NOT FOR PUBLICATION

UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

MERCK SHARP & DOHME PHARMACEUTICALS, SRL Plaintiff, v. TEVA PHARMACEUTICALS USA, INC., and TEVA PHARMACEUTICAL INDUSTRIES, LTD. Defendants.	:	Civ. No. 07-1596 (GEB)(DEA) **FINDINGS OF FACT AND CONCLUSIONS OF LAW**

TABLE OF CONTENTS

BROWN, Chief Judge

This matter comes before the Court upon the Complaint of plaintiff Merck Sharp & Dohme Pharmaceuticals, SRL ("MSD" or "Plaintiff") alleging that defendants Teva Pharmaceuticals USA, Inc. ("Teva USA") and Teva Pharmaceutical Industries, LTD ("Teva Ltd.," and together, with Teva USA "Teva" or "Defendants") infringed United States Patent No.

5,565,473 ("the '473 patent") owned by MSD. The Court conducted a non-jury trial from February 23 to February 26, 2009 and had the opportunity to observe the manner and demeanor of the witnesses and to assess their credibility. *See United States v. $33,500 in U.S. Currency*, No. 86-3348, 1998 U.S. Dist. LEXIS 19475, at *2 (D.N.J. Aug. 17, 1988). This Opinion constitutes this Court's findings of facts and conclusions of law in accordance with Federal Rule of Civil Procedure 52(a).

I. INTRODUCTION

The present litigation between MSD and Teva concerns MSD's United States Patent No. 5,565,473 ("the '473 patent"), which is entitled"Unsaturated Hydroxyalkylquinoline Acids as Leukotriene Antagonists,"and all rights therein. MSD alleges that Teva's Abbreviated New Drug Application ("ANDA") filings infringe claims 18-22 of the '473 patent under 35 U.S.C. § 271(e)(2)(A). Teva counters that the '473 patent is invalid and unenforceable because: (1) MSD acquired the '473 patent through inequitable conduct; and/or (2) the '473 patent was obvious under 35 U.S.C. § 103 in light of these additional prior arts. In addition, Teva seeks declaratory judgment from this Court that the '473 patent is invalid and unenforceable.

The parties thus proceeded to trial, and the Court now addresses their claims. The Court will first briefly recount the factual background and procedural history, before summarizing the parties' arguments at trial. The Court will also make its findings of fact and conclusions of law regarding each of the claims asserted. There are also a number of outstanding motions in limine, and the Court, where appropriate, will resolve these issues.

II. BACKGROUND

A. THE PARTIES

MSD is a restricted liability society organized under the laws of Barbados. (MSD's Proposed Findings of Fact (Revised Final Pretrial Order, Stipulated Fact 1 [Docket No. 62]). MSD is a subsidiary of Merck & Co., Inc. ("Merck")[1] (MSD's Pretrial Br. at 1 [Docket No. 70]). Teva USA is a Delaware corporation with its principal place of business in North Wales, Pennsylvania. (Revised Final Pretrial Order, Stipulated Fact 2). Teva, Ltd. is a company organized and existing under the laws of Israel having its principal place of business in Israel. (Am. Answer at ¶ 3 [Docket No. 23]). Teva USA is a subsidiary of Teva Ltd. and transacts business in the State of New Jersey and has an office in the State of New Jersey. *Id.* at ¶¶ 2, 4. Merck is the holder of approved New Drug Application ("NDA") No. 20-829 for certain dosage forms in which the active ingredient is montelukast; these products are sold under the trademark Singulair®. (Revised Final Pretrial Order, Stipulated Fact 3). MSD is the owner the '473 patent. *Id.* at 4.

B. THE PATENT-IN-SUIT

The '473 patent is the sole patent in suit. *Id.* at 23. The named inventors of the '473 patent are Michel Belley, Dr. Serge Leger, Dr. Marc Labelle, Dr. Patrick Roy, Dr. Yi B. Xiang, and Dr. Daniel Guay. *Id.* at 24. Claims 18-22 of the '473 patent cover montelukast sodium, which is the active ingredient in the Singulair® tablets, Merck's pharmaceutical product used for treating certain ailments, including asthma and allergic rhinitis. *Id*. at 32-36. Montelukast is depicted as shown in Figure 1, attached hereto in Appendix A. Before the '473 patent issued, Merck made several applications to the PTO, which were rejected by the PTO on various

[1] The Court shall use the term "Merck" to collectively refer to Merck & Co., Inc., Merck Sharpe & Dohme Pharmaceuticals, SRL, and Merck Frosst Canada. *See* Stipulated Fact 3.

grounds, including that the applications were obvious in view of certain prior art. *Id* at 69-84, 87-89. In one such application, U.S. Patent Application Serial No. 07/774,414 ("the '414 application"), filed on October 10, 1991, the PTO rejected the claims as anticipated or obvious based on U.S. Patent No. 4,851,409 ("Young '409"), stating in an Office Action dated May 26, 1992, that "Patentees' all teach the claimed quinoline derivatives" and that Young '409 disclosed examples where "Q2 is CH2-OH and Y = -CH=CH," and so disclosed compounds where Q^2 could be a primary alcohol.[2] *Id.* at 88. In a Reply and Amendment dated August 26, 1992, Mr. Gabriel Lopez, Merck's in-house patent attorney, traversed the rejection on this ground, stating that "[t]he present definitions of Z^1/Z^2 = $CONR^3$. Any one of these differences would render the present compounds unobvious; the combination of three substantial differences appears irrefutable." *Id* at 89. On December 15, 1992, the examiner issued an office action without repeating the rejection based on Young '409 and a Notice of Allowance was issued on November 28, 1994. *Id.* at 90-91. Eventually, the '473 patent issued on October 15, 1996.

On February 20, 1998, the use of Singulair® tablets in 10 mg form and 5 mg form for the prophylaxis and chronic treatment of asthma in patients 15 years of age and older and pediatric patients from 6 to 14 years of age, respectively, was approved by the United States Food and Drug Administration ("FDA"). *Id.* at 41-42.

C. PROCEDURAL HISTORY

On April 3, 2007, MSD filed two complaints in the United States District Court for the District of New Jersey, Civil Action No. 07-1596 (GEB), alleging infringement of the '473

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[2] As further discussed below, the "Q^2" side chain refers to the amide containing side chain of the compound known as L-660,711.

patent pursuant to 35 U.S.C. § 271(e)(2)(A) by Teva. *Id* at 8, 16. MSD also filed First Amended Complaints in both actions on August 6, 2007 and on On August 7, 2007, the Court ordered the two cases be consolidated. *Id*. at 19-20. The Court conducted a four day non-jury trial from February 23 to 26, 2009. (Trial Transcripts [Docket Nos. 91, 94-95, 97-98, 100, 105]).

The Court now issues this memorandum opinion pursuant to Federal Rule of Civil Procedure 52(a).

II. DISCUSSION

A. THE PARTIES' CONTENTIONS AT TRIAL

1. The Parties' Contentions Regarding Inequitable Conduct

a. Teva's Arguments Regarding Inequitable Conduct

(1) Young 89 is Highly Material

Teva avers that MSD withheld certain prior art, specifically the publication entitled "*Structural Analysis of Sulfido-Peptide Leuktorienes: Application to the Design of Potent and Specific Antagonists of Leukotriene D_4*," ("Young 89") and the model of an LTD_4 receptor that it included (the "Young 89 Model"), during the prosecution of the '473 patent with an intent to mislead the PTO. (Teva's Proposed Statement of Fact ("Teva's Proposed Facts") at 1 [Docket No. 111]; (PTX3283)). Teva also argues that Young 89 was highly material in the context of the patent prosecution. Teva's Proposed Facts at 2.

Teva alleges that: (1) the adoption of a structure containing a secondary or tertiary alcohol at the Q^2 position of the compounds was a central issue in the prosecution of the '473 patent, and (2) MSD's failure to disclose Young 89, and thus the Young 89 Model, to the PTO critically impacted the examiner's decision to grant the '473 patent. *Id*. at 2-5. Specifically, Teva notes

that the Young 89 Model identifies three parts of a leukotriene antagonist. *Id*. at 5. Teva further alleges that the Young 89 Model teaches that the group in one position, which the model indicated would bond to pocket "B" of the receptor, must possess three attributes: that group must be (1) polar; (2) not ionized; and (3) a hydrogen bond acceptor. *Id.* at 5. Teva further contends that the "B" pocket in the Young 89 Model corresponds to the Q^2 side chain in the compounds of the '473 patent. *Id*. at 6. Teva also asserts that the Young 89 Model: (1) presented important activity data, both the explicit data directed to L-660,711 and additional compounds as well as other activity data upon which the Young 89 Model was based; and (2) that it also indicated that the LTD_4 antagonist needed not only to hydrogen bond, but to also be a hydrogen bond acceptor to bond at the "B" pocket of the Young 89 Model. *Id*. at 7.

As such, Teva argues that Young 89 would have supported the examiner's rejection of the '473 patent on the basis that the secondary or tertiary alcohol are obvious substitutions for the primary alcohol at the Q^2 position in the structurally similar prior art. *Id*. at 7. According to Teva, since Young '409, which is prior art to the '473 patent, disclosed a primary alcohol at the Q^2 position, and it was known that a primary alcohol is polar, not ionized, and a hydrogen bond acceptor, a reasonable examiner would have concluded that the secondary and tertiary alcohol, which are also polar, not ionized, and hydrogen acceptors, were obvious variations. *Id*. at 8. Therefore, Teva argues that the information revealed in Young 89 would have been important to a reasonable examiner in determining the obviousness of the '473 patent because Young 89 would have "reinforce[d] his initial rejection [of the priority application that eventually matured into the '473 patent] based on the primary alcohol being equivalent to the secondary and tertiary alcohols." *Id*.

Teva also asserts that the Young 89 Model was important in the actual development of montelukast. *Id*. at 6, 8-13. Defendants assert that the Young 89 Model was used to develop one of Merck's most potent LTD_4 antagonists at the time, L660-711. *Id*. at 6. Moreover, Teva alleges that the Merck chemists working on the development of an LTD_4 antagonist acknowledged that the Young 89 Model played an important role in the decision to modify prior compounds and place a tertiary alcohol in the Q^2 position. *Id*. at 10-13.

Furthermore, Defendants argue that Young 89 was also highly material because it "would have, by itself or in combination with [prior art U.S. Patent No. 5,104,882 ("the '882 patent") and Young '409] supported a *prima facie* obviousness rejection." *Id*. at 13. Teva argues that the three necessary attributes of the Q^2 position taught by the Young 89 Model, namely that it must be: (1) polar, (2) not ionized; and (3) a hydrogen bond acceptor, are shared by the dimethyl amides found in those prior art compounds as well as in the tertiary alcohol found in the '473 patent. *Id*. at 14. Therefore, Defendants assert that these shared attributes, as disclosed by the Young 89 Model, would have led a person of ordinary skill in the art to have reasonably expected the compounds of claims 1 and 7 of the '473 patent to be active as LTD_4 antagonists. *Id.* at 16. Teva claims that Young 89 is therefore highly material because it supported a *prima facie* obviousness rejection of claims 1 and 7 of the '473 patent because "the structure of the compounds claimed in the '473 patent would have been obvious under the standards applied by the PTO during prosecution." *Id.* at 16.

To rebut the assertions of MSD's witnesses that many different substituents would meet the three requirements of the Q^2 position as taught by the Young 89 Model, Defendants argue that although a tertiary alcohol is not the only group that meets these three requirements, a

medicinal chemist could use "various tools to create a hierarchy of compatible substituents," and in doing so could determine that the use of a tertiary alcohol in the Q^2 position "would be at the top of the list." *Id*. at 14-15.

(2) Mr. Lopez was Aware of Young 89 During the Prosecution of the '473 Patent and Intentionally Withheld It from the PTO

Defendants further argue that the Court should find that Mr. Gabriel Lopez was aware of Young 89 and the Young 89 Model, during the prosecution that resulted in the '473 patent and intentionally withheld the reference from the PTO. *Id*. at 17.

Teva asserts that Mr. Lopez was Merck's in-house patent attorney and was responsible for prosecuting all of Merck's leukotriene antagonist patents. *Id.* at 3 n. 1. Defendants argue that Mr. Lopez's testimony demonstrates that he was aware of Young 89 and the Young 89 Model during the patent prosecution. *Id*. at 18. Specifically, Teva asserts that Mr. Lopez "admitted that 'at the time [he was] prosecuting the ['']473 patent" that he knew "that there was a receptor model" at Merck. *Id.* at 18 (citing T. Tr. 43:3-10, Feb. 24, 2009 A.M. (Lopez)). Teva also asserts that, although he could not recall most details of the Young 89 Model, he did remember (consistent with the disclosure of Young 89) that Merck's LTD_4 antagonist model had three points of contact with the receptor. (Teva's Proposed Facts at 18 (citing T. Tr. 43:23-44:11, Feb. 24, 2009 A.M. (Lopez))). Defendants further argues that "there is no dispute that Mr. Lopez did, in fact, review and approve for publication the Young 89 article, including the [Young 89 Model]." (Teva's Proposed Facts at 18 (citing DTX-1410; T. Tr. 22:4-23:2, Feb. 24, 2009 A.M. (Lopez))).

Defendants also assert that Mr. Lopez reviewed other papers that repeatedly reminded

him of the Young 89 Model. Teva's Proposed Facts at 18-20. Defendants note Mr. Lopez's testimony that he would have given very little review to these other papers in light of the fact that Dr. Young, the author of one such publication, had indicated that there was nothing in it that was not already approved for publication. *Id.* at 20-21. However, Defendants attempt to refute such testimony by citing the manuscript review form for Young 89, which contains a notation that "[t]he author has indicated that all of the material in this manuscript was previously cleared in 87-ms-1290." *Id*. at 21 (citing DTX-1410 at MSD02113350). Teva asserts that Mr. Lopez's handwritten note, in which he comments "NO – 1290 was an abstract only," indicates that Mr. Lopez did not take this manuscript at face value but instead carefully reviewed it as well as other manuscripts that included the Young 89 Model. *Id.* (citing DTX-1410 at MSD02113350).

With respect to Mr. Lopez's intent to deceive the PTO, Teva argues that MSD and Mr. Lopez have offered no explanation, based on any contemporaneous evidence, for the failure to provide Young 89 to the PTO after the examiner focused the prosecution on the distinction between the primary alcohol in the prior art and the tertiary alcohol in the pending claims. *Id.* at 17. Rather, Defendants assert that MSD asks the Court to infer that Mr. Lopez's failure to disclose Young 89 was result of oversight, because he cannot recall, today, anything about a decision not to disclose Young 89 during the patent prosecution. *Id.* Teva argues that although Mr. Lopez testified that he would never intentionally withhold material information from the PTO, such a speculative assertion, with no supporting facts or memory, is not legally sufficient to explain the failure to disclose such a highly material reference as Young 89. *Id.*

(3) Mr. Lopez was Aware that Young 89 was Highly Material

Defendants further allege that not only was "Mr. Lopez aware of Young 89 and [the

Young 89 Model], but he also knew or should have known of the high materiality of this information." *Id*. at 22. Noting Mr. Lopez's training in chemistry and experience with patent prosecution, especially with patents related to leukotriene antagonists, Teva argues that Mr. Lopez must have known the significant importance and materiality of Young 89. *Id*. at 22-23. Defendants also aver that Mr. Lopez understood his duty of candor to the PTO and that such a duty required him to disclose material information, during prosecution. *Id*. at 23. Finally, Teva argues that Mr. Lopez's involvement in the patent prosecution process also enabled him to understand the importance of the '473 patent to Merck it work to produce a leukotriene antagonist. *Id*. at 24. In light of the foregoing, Defendants urge the Court to conclude that Mr. Lopez withheld the Young 89 Model with the intent to deceive the PTO and therefore hold the '473 patent unenforceable. *Id*.

b. MSD's Arguments Regarding Inequitable Conduct

Plaintiff maintains that Young 89 is not material to the prosecution of the patent. (MSD's Proposed Facts at ¶¶ 479-481). In addition, Plaintiff denies that the failure to disclose Young 89 was intentional. *Id.* at ¶ 482.

(1) Young 89 is Not Material

MSD avers that Young 89 is not material to the patentability of the '473 patent. *Id*. at ¶ 490. Plaintiff argues that Young 89 is "very broad and very noninformative" because the Young 89 Model does not address many other factors such as: (1) the steric requirements; (2) the shape of the receptor; (3) the requisite polarity to bind with the receptor; (4) and the directionality of potential hydrogen bonds. *Id*. at ¶ 491. Additionally, MSD asserts that the Young 89 Model would not be useful in drug design and "would not provide any guidance as to distinguishing

between any of the huge number of potential compounds that fit the model." *Id*. at ¶ 503. Plaintiff maintains that Merck developed "many compounds that fit loosely within the Young 89 [M]odel but failed as effective and safe LTD_4 antagonists." *Id*. Moreover, MSD asserts that Young 89 and the Young 89 Model were presented by Dr. Young at a conference in Taipei and so were available outside for review and use to those not involved with Merck's Leukotriene Program. *Id*. at ¶¶ 240-242.

Specifically, Plaintiff avers that Young 89 does not suggest the use of a tertiary alcohol in the Q^2 position of a proposed LTD_4 antagonist. *Id*. at ¶ 509. MSD maintains that the scientist who had the idea to use a tertiary alcohol, Mr. Belley, was not motivated by the Young 89 Model. *Id*. ¶ 510. According to Plaintiff, other Merck scientists working to discover an LTD_4 antagonist, including Dr. Young, also did not think a tertiary alcohol would work. *Id*. In addition, Plaintiff points out that Dr. Labelle, another Merck scientist and a listed co-inventor of the '473 patent, testified that he never used the Young 89 model in designing backup compounds to MK-571. *Id*. at ¶ 515. Finally, MSD avers that competitors of Merck, such as Smith Kline & French (SK&F), failed to develop a safe and effective leukotriene antagonist. *Id*. at ¶ 522.

(2) Mr. Lopez Did Not Make Any False Statements to the PTO

MSD asserts that Mr. Lopez was employed by Merck as a patent attorney from approximately 1977 to 1993 and that during his period of employment, he wrote and prosecuted several patent applications, including the patents to which the '473 patent claims priority, but that he did not file or prosecute the '473 patent. *Id.* at ¶¶ 484, 489.

Plaintiff also argues that Mr. Lopez did not make any false or misleading statements to the PTO. Specifically, Plaintiff points to Mr. Lopez's response to the patent examiner's rejection

of the '414 application as obvious over Young '409, in which he states that "'[t]he present compounds differ from the art in that Q^2 is a secondary or tertiary alcohol or amine and that the present $Z^1/Z^2 = CONR^3$. Any one of these differences would render the present compounds unobvious; the combination of three substantial differences appears irrefutable.'" *Id.* at ¶ 526 (citing TEX 1444.0609). MSD argues that the trial testimony of Dr. Lenz, Teva's expert witness on obviousness, supports Mr. Lopez's assertion that the compounds differ in a relevant ways. (MSD's Proposed Facts at ¶¶ 527-529 (citing Dr. Lenz's testimony that primary alcohols and secondary or tertiary alcohols differ in both chemical and metabolic ways). Merck further argues that, tertiary alcohols differ from primary alcohol in terms of reactivity, stability, polarity and size. *Id*. at ¶¶ 534-539. Noting that Mr. Lopez's response to the patent examiner does not specify on what grounds he is differentiating the secondary and tertiary alcohols in the '414 application and instead states that "'[t]he present compounds differ from the art'" in question based on the presence of secondary and tertiary alcohols, MSD argues that, in light of the foregoing, it cannot be stated that Mr. Lopez's statements to the PTO are untrue. *Id.* at ¶¶ 539-540 (quoting TEX 1444.0609). As such, MSD asserts that "Mr. Lopez's statements were nothing more than attorney argument to the patent examiner and should not be subject to the severe penalty of inequitable conduct." (MSD's Proposed Facts at ¶ 542).

(3) Mr. Lopez Did Not Intend to Deceive the PTO

MSD further argues that Mr. Lopez did not at any time during his work relating to the prosecution of the '473 patent have an intent to deceive the PTO in any way. *Id.* at ¶ 543. Plaintiff asserts that there are "at least two 'perfectly valid reasons' why Mr. Lopez would not have attempted to deceive the PTO: (1) 'it would be against the law and [Mr. Lopez is] an

attorney and [he] wouldn't have done that" and (2) Mr. Lopez "wouldn't risk [his] license on the basis . . . [of] doing something as idiotic as attempting to deliberately hide a document." *Id.* at ¶ 544 (quoting T. Tr., Feb. 24, 2009 A.M. 63:22-64:15 (Lopez)).

In addition, Plaintiff points to the testimony of various scientists and patent agents, including Mr. Belley, Dr. Guay, Dr. Xiang, Dr. Leger, involved in Merck's work on leukotriene antagonists to support the proposition that no one involved in the prosecution of the '473 patent had knowledge of Young 89 during the prosecution of the patent. *Id*. at ¶¶ 545-559. As to Mr. Lopez, Plaintiff avers that he reviewed "probably 100 or more [manuscript approvals] on an annual basis" and that made up only a small part of Mr. Lopez's job responsibilities. *Id*. at ¶¶ 564-565. Therefore, MSD asserts that "Mr. Lopez sometimes read less of a proposed manuscript if there were indications that suggested to him that approval of the manuscript would not be problematic." *Id*. at ¶ 565. MSD further notes that Mr. Lopez testified that some of the factors that would influence the amount of time that he would devote to certain manuscripts were whether: (1) the author, especially an author that Mr. Lopez trusted, indicated that there was nothing in the manuscript that had not been approved before; (2) a patent had been issued regarding the subject matter of the manuscript; or (3) a patent application had been filed regarding the subject matter of the manuscript. *Id.* at ¶ 566. As to the several manuscripts which Mr. Lopez reviewed and which included the Young 89 Model as well as the manuscript of what was eventually published as Young 89, MSD asserts that Mr. Lopez testified that either: (1) he did not recall whether he specifically saw or paid attention to the depiction of the LTD_4 receptor model in the figures attached to the back of the manuscript; or (2) he did not recall the line of inquiry that led him to understand that all of the material included in a certain manuscript could

not have been cleared in the previous publication when he made notations to that effect. *Id.* at ¶¶ 568-602. MSD further argues that other manuscripts that included references to Young 89 or the Young 89 Model did so without identifying the model as the Young 89 Model and without further elaborating on its properties. *Id.* at ¶¶ 582-602.

In light of the foregoing, MSD asserts that: (1) Mr. Lopez did not necessarily review these publications in detail due to his heavy workload and Dr. Young's position; (2) while he did approve for release a manuscript of what was eventually published as Young 89, this approval occurred more than two years before the filing date of '887 application, the earliest continuation-in-part to which the '473 patent claims priority; and (3) Mr. Lopez does not recall ever considering whether or not to disclose Young 89 to the PTO during the prosecution of the '473 patent or of making a conscious decision to do so or not to do so. *Id.* at ¶¶ 612, 614, 616.

MSD also argues that Mr. Lopez understood that he had an obligation to disclose information to the PTO that was material to the patentability of pending claims during his work on the prosecution of the '473 patent. *Id.* at ¶ 617. MSD asserts that, by disclosing several references to patents listing Dr. Young as an inventor, Mr. Lopez complied with his duty of candor and that, given such disclosures, there is no reason to believe that Mr. Lopez would have tried to hide a document that would be easily discoverable later. *Id.* at ¶¶ 619-620.

2. The Parties' Contentions Regarding Obviousness

a. Teva's Arguments Regarding Obviousness

Defendants allege that claims 18-22, which cover montelukast, particular salts, and the methods of using the drug, are obvious under 35 U.S.C. § 103. (Teva's Proposed Facts at 25).

(1) Defining a Person of Ordinary Skill in the Art

Noting that obviousness is determined from the point of view of a person of ordinary skill in the art, or a hypothetical person whom the law presumes has knowledge of all prior art references in the field of the invention in the relevant time frame, and that because claims 18-22 are entitled to a priority date no earlier than August 8, 1991 and therefore the relevant time frame for the obviousness inquiry is 1990 to 1991, Teva argues that the following definition of a person of ordinary skill in the art should be used in the instant case:

> A person of ordinary skill in the art in 1990 to 1991 would be a Ph.D. medicinal chemist or an organic chemist with a minimum of two years of experience in drug discovery, design, development and an understanding of biological assays. The person would not necessarily have experience working with leukotriene antagonists to begin with but would have brought themselves up to speed before commencing work.

Id. at 25-26. Defendants then assert that Dr. Lenz, Teva's obviousness expert, fits this definition because "[j]ust like any medicinal chemist with general drug development experience, [he] brought himself up to speed in the leukotriene area by reviewing the prior art, including literature, patents and patent publications." *Id.* at 26.

(2) Relevant Prior Art Disclosing LTD_4 Antagonists

After summarizing the general approach a medicinal chemist would take to develop an LTD_4 antagonist, Teva summarizes the prior art on for such antagonists and includes as relevant prior art: (1) Young 89; (2) Young '409; (3) the '882 patent; (4) Merck's European Patent EP 318,093 ("Young '093"). *Id*. at 26-28. Teva asserts that Young 89 disclosed that Merck used the Young model to develop L-660,711, which was one of the most potent LTD_4 antagonists known at the time. *Id.* at 27. Teva also notes that Young '409 disclosed and patented L-660,711. *Id*. at 28. Teva further contend that L-660,711 presents the two side chains – Q^1 and Q^2, where the acid

chain is at the Q^1 position and the dimethyl amide chain is at the Q^2 position. *Id*. at 28. Defendants assert that Q^1 and Q^2 side chains are not interchangeable. *Id*. at 30.

(3) Teva's Lead Structure

Defendants argue that a lead structure can be constructed based on L-660,711, a compound created by Merck during its attempts to develop a commercially useful leukotriene antagonist, under the teachings of Young 89, and incorporating changes made by Merck in the '882 patent and Young '093. *Id*. at 29-30. Specifically, Defendants contend that these prior art would suggest to a person of ordinary skill in the art that a phenyl ring should be added to the Q^2 side chain, resulting in a lead structure that is consistent with the Young 89 Model. *Id*. at 30. Then, Teva asserts that, of the compounds disclosed in the '882 patent, a person of ordinary skill in the art would have chosen Compound 97 of the '882 patent as a particularly preferred compound. *Id*. at 30. Compound 97 uses a dimethyl amide at the end of the Q^2 chain, where the lead structure does not identify a particular group. *Id*. at 30-31. Defendants assert that this modification is justified because L-660,711, which was proved to possess superior properties, has a dimethyl amide at the end of the Q^2 chain. *Id*. at 31.

Defendants further argue that the Q^1 chain should be homologated by adding a methylene group because homologation is standard operating procedure for a medicinal chemist. *Id*. at 31. According to Teva, to prevent beta-oxidation, a Person of ordinary skill in the art would put either two methyl groups or a cyclpropyl group in the beta position. *Id*. at 31. After making such modifications to the Q^1 chain, Defendants argue that a Person of ordinary skill in the art would substitute the dimethyl amide on the Q^2 chain with an acceptor that possesses the three attributes taught by Young 89 or one that is: (1) polar; (2) non-ionized; and (3) a hydrogen bond acceptor.

Id. at 32. Teva asserts that a tertiary alcohol would be one of the first groups a medicinal chemist would try. *Id*. at 32-33. Finally, Defendants argue that a Person of ordinary skill in the art would recognize that the compound resulting from the modifications outlined above would be a racemate, a mixture of enantiomers and that a Person of ordinary skill in the art would follow the prior art and separate the resulting racemate. *Id*. at 33. Defendants assert that the resulting compound is montelukast, which is covered by Claim 18 of the '473 patent. *Id*. These steps are depicted as shown in Figure 2, attached hereto in Appendix A.

In light of the foregoing, Defendants assert that Claim 18 is obvious and Claims 19-22, which cover the sodium salt of montelukast, a pharmaceutical composition using montelukast, and using montelukast as a leukotriene antagonist, or to treat asthma, respectively, are also obvious. *Id*.

(4) Teva's Arguments Regarding Secondary Considerations

Defendants further allege that MSD's evidence of secondary considerations is insufficient to overcome the structural obviousness of montelukast. *Id*. at 34.

(a) Singulair® Does Not Provide Superior Asthma Relief

Defendants argue that Singulair® does not provide superior asthma relief. *Id*. Defendants asserts that inhaled steroids are more effective in asthma treatment than Singulair® and so "Singulair® . . . does not answer any unaddressed need for new asthma therapies that was present in 1990 to 1991 or even today." *Id*. at 34-35. Teva also avers that Singulair® does not provide superior relief for allergic rhinitis because "the preferred treatment for allergic rhinitis is topical steroids." *Id*. at 35.

(b) Merck's Extensive Promotion of Singulair® Contributed to Its Commercial Success

Defendants further argue that Merck's extensive promotion contributed to Singulair®'s sale. *Id*. at 36. Defendants assert that Merck has spent more than [AMOUNT REDACTED][3] on marketing and promotional activities with respect to Singulair® products aimed at both consumers and doctors. *Id*. at 36-37. Relying on expert witnesses and Merck's internal documents, Defendants allege that the sale of Singulair® is largely due to successful promotions, instead of effectiveness of the drug. *Id*. at 37-38. Specifically, Teva disputes the testimony of Dr. Christopher A. Vellturo, Merck's expert witness on the relationship between the commercial success of Singulair® tablets and the properties of montelukast, in which Dr. Vellturo stated that Merck's promotional advertising to consumers and doctors provided nothing more than information on the benefits of Singulair®. *Id.* at 37. Teva argues that Dr. Vellturo is not an expert in marketing or in promotional messaging, nor does he have any training to evaluate the psychological aspects of the Singulair® advertisements that he reviewed. *Id.* Further, Teva asserts that Dr. Vellturo's cursory review of Merck's direct-to-consumer ("DTC") advertising involved only a review of storyboards of television advertisements for Singulair® and not the actual television commercials for Singulair® despite the fact that the majority of Merck's DTC advertising, consisted of television ads. *Id.* at 37-38. Defendants also argue that Merck's internal documents show that Merck's promotional activities caused physicians to prescribe more Singulair®. *Id.* at 38.

b. MSD's Arguments Regarding Obviousness

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[3] Redacted pursuant to Order Granting Teva's Motion to Seal, entered April 21, 2009 [Docket No. 116].

In recounting Merck's efforts to develop a safe and effective LTD_4 antagonist and the complications and surprises it contends Merck faced during the process, Plaintiff argues that Teva's obviousness analysis is without merit.

(1) Teva Cannot Change Its Definition of a Person of Ordinary Skill in the Art to Fit Dr. Lenz's Experience

Plaintiff asserts that Teva is impermissibly attempting to change its own definition of one of ordinary skill in the art. (MSD's Proposed Facts at ¶ 185). MSD notes that Teva's paragraph IV certification notice included the following definition of the level of skill in the art:

> The prior art demonstrates a reasonably high level of skill. One of ordinary skill in the art would possess substantial training in chemical and biological sciences with a Ph.D. or equivalent degree, training in the areas of synthetic organic chemistry, pharmacology or a related field, and experience *working in research and development of leukotriene antagonists and leukotriene biosynthesis inhibitors*. This person would have familiarity with the classes of leukotrienes, structure/function relationships of small molecule binding to the leukotriene receptors as well as standard assays in the art for determining in vivo activity as both leukotriene antagonists or leukotriene biosynthesis inhibitors. Such an individual would easily have understood the prior art references and have the capacity to draw inferences from them.

Id. at ¶ 186 (citing TEX 3005.0006-0007) (emphasis added). MSD also argues that Teva reiterated this position as the level of skill in the art in its Supplemental Response to Merck's Interrogatory No. 11. *Id.* at ¶ 187.

MSD argues that Dr. Lenz does not fit this definition of a Person of ordinary skill in the art., noting that Dr. Lenz testified that he "does not have the 'experience working in research and development of leukotriene antagonists' required by Teva's definition." *Id.* at ¶ 188 (citing T. Tr., Feb. 24, 2009 A.M. 136:3-5, 137:15-20). MSD asserts that, after hiring Dr. Lenz to conduct Teva's obviousness analysis, Teva submitted a new definition of one of ordinary skill in the art in

the Revised Final Pretrial Order, which omits any reference to a person of ordinary skill in the art having experience in the art of designing leukotriene antagonists:

> As of October 12, 1990, the hypothetical person having ordinary skill in the art of the '473 patent would possess a reasonably high level of skill. One having ordinary skill in the art would possess substantial training and experience in medicinal chemistry, experience or training in the chemical and biological sciences with a Ph.D. or equivalent degree in chemistry, experience or training in synthetic organic chemistry, and at least two years of experience in drug discovery, design, testing, and development. Such a person would have understood the prior art references and have the capacity to draw inferences from them, individually and overall, in designing LTD_4 antagonists.

Id. at ¶ 189 (citing Revised Final Pretrial Order at 54, ¶ 98). MSD asserts that its own definition of a person of ordinary skill in the art, which requires that one of skill in the art should have several years of experience working in the field of leukotriene antagonists, is the appropriate definition:

> One of ordinary skill in the art should be understood as someone with substantial training in the chemical and biological sciences with an advanced degree in chemistry, training in the areas of synthetic organic chemistry and medicinal chemistry, and substantial experience working in the research and development of leukotriene antagonists.

Id. at ¶ 191 (citing Revised Final Pretrial Order at 24, ¶ 99).

Plaintiff asserts that its own expert on obviousness, Dr. John G. Gleason, fits this definition of a Person of ordinary skill in the art because he: (1) was involved in SK&F's LTD_4 antagonist program since before the discovery of the leukotrienes; (2) was one of the originators of SK&F's leukotriene program; and (3) was either a Program Leader or Co-Leader of that program for its entire duration, which lasted from late-1979/early-1980 through the early 1990s. *Id.* at ¶ 193. Further, Plaintiff argues that Dr. Gleason attended many conferences or meetings

related to leukotriene antagonists and was also invited to speak at many of them as well. *Id.* at ¶ 201.

In contrast, MSD argues that Dr. Lenz, in addition to not having experience working in research and development of leukotriene antagonists: (1) read only about 50 articles, some of which were published after the 1990 to 1991 timeframe, in order to educate himself in the field before rendering his opinion; (2) agrees that a publication, "Leukotriene Receptors," appearing in *Comprehensive Medicinal Chemistry* and written by W. Kingsbury and others, including Dr. Gleason ("the Kingsbury publication") sets out the state of the art in 1990 fairly accurately; and (3) did not attend any conferences or meetings related to leukotriene antagonists and did not speak to anyone who had. *Id.* at ¶¶ 198-200. Merck further notes that for at least the last 14 months, Dr. Lenz has worked mostly as a consultant in litigations, not a medicinal chemist. *Id.* at ¶ 202. As such, MSD implies that Dr. Lenz does not even meet Teva's revised definition of a person of ordinary skill in the art. *Id*. at ¶¶ 198-200, 202.

(2) Teva's Choice of a Lead Compound is Flawed

MSD asserts that Teva has "incorrectly defined the "problem" to be addressed in its obviousness analysis in terms of the solution addressed by the '473 patent." *Id.* at ¶ 204 (citing Teva's Pretrial Brief at 31 [Docket Entry No. 73] which states that the appropriate obviousness analysis that begins with an assertion that "[t]he problem addressed by the '473 patent was to identify additional quinoline-based LTD_4 antagonists"). Plaintiff asserts that a Person of ordinary skill in the art would have been motivated to examine a variety of compound structures, not just quinoline-based antagonists and that by April 1991, a person of ordinary skill in the art "would have been aware of at least ten compounds in the area of leukotriene antagonists that

were in preclinical or clinical evaluations," for which there was biological assay data and that only five of those ten compounds were quinoline based. (MSD's Proposed Facts at ¶ 205-207). MSD further asserts that Dr. Lenz testified that he would have been aware of these compounds and that the compounds exhibited desirable properties and that a Person of ordinary skill in the art would look to this data because drug discovery is based on data. *Id.* at ¶ 208. However, MSD asserts that Teva has offered no explanation as to why a Person of ordinary skill in the art would have chosen its hypothetical lead compound, for which there is no clinical data available, over one of these actual compounds. *Id.* As such, Plaintiff argues that there is no obvious reason for Teva to begin its analysis with a Merck compound as a lead compound. *Id.* at ¶ 210.

(3) Teva's Obviousness Analysis Was Conducted Without the Benefit of Data

MSD asserts that, in conducting his analysis, Dr. Lenz did not take any data into account in the generation of his intermediate structures but instead made all of the changes to get from his lead compound structure to montelukast without the benefit of any assay data. *Id.* at ¶ 216. As such, MSD contends that Dr. Lenz admitted that his analysis begins with L-660,711 and takes eleven distinct steps to arrive at montelukast, "all of which is accomplished without the benefit or support of any biological data." *Id*. at ¶ 217.

As such, Plaintiff asserts that Teva used hindsight and ignores several other possible lead compounds in its obviousness analysis. MSD notes that Dr. Lenz testified that he applied four filters to come up with his lead compound structure, found that compound 97 would have been particularly preferred because of the dimethyl amide at the "X" position of his generic lead structure, and that he looked to the '882 patent to see if there were any other compounds that satisfied his filters. *Id.* at ¶¶ 223-226. MSD asserts that Dr. Lenz nevertheless ignored the fact

that compounds 402, 409, 410, and 420 of the '882 patent also satisfy his four filters, even when the preferred and more restrictive criteria that "X" be a dimethyl amide is applied. *Id.* at ¶ 227. MSD further concludes that "Dr. Lenz cherry-picked, with the benefit of hindsight, those compounds with structures that he perceived to require the fewest modifications to get to montelukast," arguing that, of the ten compounds that actually satisfy his four filters, Dr. Lenz chose to ignore all those that required additional steps to result in montelukast. *Id.* at ¶ 232.

(4) The Young 89 Model

Plaintiff next addresses the relevance and materiality of the Young 89 Model to the design of chemical compounds.

(a) The Young 89 Model Had Been Presented to the Public

Plaintiff asserts that the Young 89 Model was presented at the Taipei conference in 1989 and included in Young 89 was "Dr. Young's attempt to bring together in a pictorial representation information already known in the publicly available literature from Merck's own work and from other's work" and that "Dr. Young intended his Taipei presentation and 1989 paper to be a review of the research conducted in the field up to that time." *Id.* at ¶ 242.

(b) The Young 89 Model is Too Crude to Provide Guidance in the Development of an LTD_4 Antagonist

Plaintiff argues that Young 89 does not address many potential chemical attributes that are required for an effective LTD_4 antagonist, including steric requirements, the shape of the receptor, the requisite polarity to bind with the receptor, and the directionality of potential hydrogen bonds. *Id*. at ¶ 244. Moreover, Plaintiff points to the testimony of several scientists involved in Merck's Leukotriene Program and the discovery of the '473 patent, including Mr.

Belley, Drs. Xiang, Guay, Labelle, Leger, Young and Robert Zamboni that many–"millions of" or "an infinity of"–compounds could fit the Young 89 model. *Id*. at ¶¶ 243-256.

Plaintiff further argues that: (1) the Young 89 Model does not suggest that an alcohol would be desirable as a side chain substituent in that it does not even mention alcohols, *Id.* at ¶ 265; (2) the Young 89 Model does not teach that a primary alcohol would be interchangeable with either a secondary or a tertiary alcohol because, as several of MSD's witnesses noted, tertiary alcohols differ from primary alcohols in various important ways, *Id.* at ¶¶ 265-274; (3) the Young 89 Model does not suggest a tertiary alcohol would be interchangeable with a dimethyl amide due to their differing sizes and shapes, *Id.* at ¶¶ 275-79; and (4) the Young 89 Model does not suggest that the Q^1 side chain must terminate in a carboxylic acid, *Id*. at ¶¶ 280-281.

(c) The Filters Teva Used to Arrive at Its Lead Compound Structure are Flawed

In addition to a general denial to the materiality of Young 89, Plaintiff provides specifically rebuts Teva's modifications and alterations of L-660,771 which resulted in its lead compound.

Specifically, Plaintiff alleges that: (1) there is no evidence to support the assertion that the linker group connecting the central phenyl ring and the quinoline must contain a double bond, *Id.* at ¶¶ 282-286; (2) there is no convincing basis, including the Young 89, Young '409, nor the '882 patent, to place a carboxylic acid on the Q^1 side chain and that there is no rational basis to attach the "X" substituent of Teva's generic lead compound to the ortho-position of the Q^2 phenyl ring, *Id.* at ¶¶ 287-301; and (3) the placement of a phenyl ring on the Q^2 side chain is not supported by data nor any suggestion in the literature that doing so would be a good idea. *Id*. at

¶¶ 302-303.

(d) Teva's Modifications of Its Lead Compound Structure are Also Flawed

MSD also argues that Young 89's teaching would not lead a person of ordinary skill in the art to choose a tertiary alcohol at the Q^2 side chain because 30 to 40 classes of substituents would satisfy the criteria of the Young 89 Model for the "X" position in the Q^2 side chain. *Id.* at ¶ 307. Plaintiff further notes that the publication "*Synthesis and LTD_4 Antagonist Activity of 2-Norleukotriene Analogues*," written by Thomas W. Ku and others, including Dr. Gleason (the "Ku Paper"), focuses on research done regarding the SK&F compounds and would have been available to one of ordinary skill in the art at the time of the invention. *Id.* at ¶ 315. MSD asserts that the Ku Paper teaches that when SK&F scientists inserted an alcohol in what has been referenced in this litigation as the Q^2 side chain, the resulting compound actually showed decreased activity relative to a corresponding compound with a carboxylic acid at the Q^2 position. *Id.* at ¶ 317.

Moreover, Plaintiff argues that the Young 89 Model does not suggest that a tertiary alcohol is interchangeable with a dimethyl amide. Relying on the testimony of Dr. Young, MSD avers that a tertiary alcohol is a less likely candidate because it is too lipophilic and less polar than an amide. *Id*. at ¶ 331, 333-334. In addition, Plaintiff argues that there is no rational basis to lengthen the Q^1 side chain. Plaintiff believes that based on the information available at the time, a Person of ordinary skill in the art would actually likely be discouraged from increasing the length of the Q^1 side chain because the article "*Synthesis and LTD_4-Antagonist Activity of Desamino-2-Nor- Leukotriene Analogues*," written by Carl D. Perchonock and others, including Dr. Gleason ("the Perchonock Paper"), which focuses on research done regarding the SK&F

compounds and which was available during the relevant time period, teaches that, when the SK&F scientists "increased the length of the side chain corresponding to the Q^1 side chain to three carbons – '[j]ust like the side chain in [Dr. Lenz's] lead structure' – the intrinsic *contractile* activity of the compound doubled" and that "Dr. Lenz admitted that this is 'not a desirable result' and 'does not indicate that adding a carbon would do any good.'" *Id.* at ¶¶ 341-342.

Finally, MSD argues that a person of ordinary skill in the art would not have been concerned about beta-oxidation of the Q^1 side chain. Plaintiff notes that the publication "In Vivo *Metabolism of the Leukotriene Receptor Antagonist, 5-(2-Dodecylphenyl)-4,6-Dithianonanedioic Acid (SK&F 102,081) in the Guinea Pig,*" written by John F. Newton and others, including Dr. Gleason ("the Newton Paper"), focuses on research done regarding an SK&F compound and would have been available to one of ordinary skill in the art at the time of the invention. *Id.* at ¶ 348. MSD further argues that the SK&F compound examined in the Newton Paper includes very similar side chain to that of the Q^1 side chain of the Dr. Lenz's compound but that "[d]espite following all paths of metabolism that this compound undergoes in the body of an animal, Dr. Lenz admits that the Newton Paper does not show any beta-oxidation of the Q^1 side chain." *Id.* at ¶ 349. Similarly, another article that was available during the relevant time period, "*Pharmacologic and Pharmacokinetic Profile of SK&F S-106203, a Potent, Orally Active Peptidoleukotriene Receptor Antagonist, in Guinea Pig*," written by D. W. P. Hay and others, including Dr. Gleason ("the Hay Paper"), focuses on research done regarding another SK&F compound, also does not show any evidence of beta-oxidation on the Q^1 side chain. *Id.* at ¶¶ 353-354. Plaintiff further asserts that beta-oxidation of the Q^1 side chain is further belied by the fact that, as Dr. Gleason testified, a person of ordinary skill in the art would not have tried to

substitute cyclopropyl group for the two methyl groups on the Q^1 side chain in order avoid beta-oxidation, as suggested by Dr. Lenz, because during the relevant time period, cyclopropyl groups were difficult to make and therefore were not commonly used. *Id.* at ¶ ¶ 356-357.

(5) Secondary Considerations

Plaintiff asserts that, even if the Court determines that Teva has established a *prima facie* case of obviousness as to claims 18-22 of the '473 patent, the secondary considerations present in this case warrant a finding of nonobviousness. *Id.* at ¶ 358.

(a) Singulair®'s Commercial Success Reflects the Benefits of the Invention

Plaintiff argues that Singulair® is a significant commercial success, noting that "sales of Singulair® pharmaceutical products from 1998, the year it was first introduced, through 2007 totaled some $14 billion dollars." *Id*. at ¶ 362. As evidence that this success is a result of the benefits of the invention, Merck notes that as sales of Singulair® products increased sales of Accolate®, the only other leukotriene antagonist that has been approved for sale by the FDA, decreased, suggesting that Singulair® is preferred over Accolate®. *Id.* at ¶¶ 369-372. MSD also asserts that "Merck spends less on advertising Singulair® than some of Merck's competitors do in advertising competing products." *Id*. at ¶ 388. In fact, Plaintiff argues, according to Dr. Jaffe, Teva's expert witness, Merck's advertising return on Singulair® products is much lower than the return received by pharmaceutical companies on average on asthma and allergic rhinitis medications. *Id*. at ¶ 391. Merck also notes Dr. Jaffe's testimony that, in developing his opinions, Dr. Jaffe did not examine Singulair® advertisements to determine whether they were informational or persuasive. *Id.* at ¶ 383. Merck also contends that the fact that doctors may have attended educational dinners that discussed Singulair® is not evidence that new prescriptions are

resulting from anything other than the intrinsic and unique properties of Singulair®. *Id.* at ¶ 385. To support this contention, Merck points to Dr. Eli O. Meltzer's, Merck's medical expert, testimony that educational dinners "are very informative" and explained that he has been a speaker at a number of such dinners over the years as a way of sharing his deep commitment to his practice and his patients. *Id.*

(b) Teva Copied Singulair® Because it is Inventive

Furthermore, Plaintiff alleges that Teva copied Singulair® because it is inventive. Plaintiff points out that for its proposed montelukast sodium and chewable tablets, Teva submitted with ANDA Nos. 78-605 and 78-723 almost the identical labeling and package inserts as those contained in corresponding Singulair® products. *Id.* at ¶¶ 394-397.

(c) Singulair® Met a Long-Felt but Unsolved Need

Plaintiff also argues that Singulair® met a long-felt but unsolved need because all the other drugs during the relevant time period showed significant shortcomings in effectively treating asthma and allergic rhinitis. Specifically, MSD asserts that: (1) short-acting beta agonists are only useful as "rescue" medication but not suitable for long term treatment, *id.* at ¶¶ 407-410; (2) inhaled corticosteroids are not particularly effective at lower doses and can cause severe side effects at higher doses, *id.* at ¶¶ 412-413; and (3) long acting beta agonists, which carry a "black box" warning indicating that they have side effects that are associated with increased chance of death, are never used on their own and are always used in conjunctions with inhaled corticosteroids, *id.* at ¶¶ 416-417.

Plaintiff also notes that Dr. Meltzer, Merck's medical expert, opined on the efficacy of Singulair® in treating asthma and allergic rhinitis. MSD notes that Singulair® tablets are the only

LTD_4 antagonist currently on the market that is indicated for once-a-day use and that montelukast is orally active and therefore there is no need to administer through the use of inhalers. *Id.* at ¶¶ 430-431. According to Dr. Meltzer, these are important attributes because they make Singulair® a drug that is easy to take and useful in the treatment of children. *Id.* at ¶¶ 430, 432. MSD also asserts that these attributes make Singulair® safer and more effective than the only other drug targeting the LTD_4 mediator: zafirlukast, sold under the trade name Accolate®. *Id*. at ¶ 436. Plaintiff avers that Singulair® is also safer than zilutin, which is a leukotriene inhibitor that is a commercially available under the name Zyflo®, which is associated with significant liver toxicity issues. *Id.* at ¶ 438.

MSD further asserts that Singulair® filled a need as alternative treatment for both asthma and allergic rhinitis medications. Specifically, Plaintiff notes that the Global Initiative For Asthma ("GINA") guidelines recommend the use of montelukast as an accepted management therapy for the treatment of asthma. *Id.* at ¶ 447. Further, Plaintiff asserts that "*Oral Montelukast, Inhaled Beclomethasone, and Placebo for Chronic Acid*," written by Kerstin Malmstrom and others ("the Malmstrom Paper"), which compares the clinical benefits of montelukast to that of beclomethasone, an inhaled corticosteroid, demonstrates that although Dr. Peter J. Barnes, Teva's medical expert, may be correct that inhaled corticosteroids are more effective than montelukast for the majority of patients, that is not true for all patients. *Id.* at ¶ 448. MSD further notes that montelukast is sometimes used as an add-on therapy to inhaled corticosteroids for patients whose asthma cannot be controlled with inhaled corticosteroids alone and that the publication "Effect of Montelukast on Exhaled Leukotrienes and Quality of Life in Asthmatic Patients," written by Wojciech A. Biernacki and others, including Teva's medical

expert Dr. Barnes (the "Biernacki Paper"), concludes that the addition of montelukast to the therapy of patients whose asthma was otherwise uncontrolled with the use of corticosteroids alone resulted in a significant improvement in patients' quality of life. *Id.* at ¶¶ 450-451.

(d) Montelukast Exhibits Many Unexpected Results

Recounting how montelukast was developed, Plaintiff also asserts that the process exhibits many unexpected results, especially regarding the adoption of a tertiary alcohol by Mr. Belley, a listed inventor of the '473 patent. Specifically, MSD points to Mr. Belley's testimony that Dr. Zamboni told him that he would be "wasting his time" with a tertiary alcohol and that, after Mr. Belley synthesized a compound containing a tertiary alcohol, "everybody was surprised to see its activity." *Id.* at ¶ 454-456 (quoting Belley Dep. Tr. 37:7-15, 54:18-24). MSD further noted that several scientists involved in the Leukotriene Program, including Mr. Belley, Drs. Zamboni, Guay and Young, found the effectiveness of the tertiary alcohol surprising because: (1) it is only slightly polar; and (2) is not hydrophilic but rather is lipophilic. (Merck's Proposed Facts at ¶¶ 457-465.

(e) Many Failed in their Efforts to Develop LTD_4 Antagonists

Plaintiff also argues that other companies also attempted to develop LTD_4 antagonists that are effective and safe enough for commercial use. *Id*. at ¶ 473. MSD asserts that, during 1990 to 1991, SK&F developed two promising compounds and licensed another from Ono Pharmaceutical and that each of these compounds progressed to clinical trials, but that they were eventually abandoned for failing to meet expectations. *Id.* at ¶¶ 473-477. Plaintiff also notes that, during this time period, several other companies, including Eli Lilly & Co., Revlon, Rhone-Poulenc Rorer, Wyeth Pharmaceuticals, Leo Pharmaceuticals, Merck, and Imperial Chemical

Industries ("ICI") had compounds in advanced stages of development and that, of all of these compounds, only the ICI compound, eventually made it to commercial development. *Id.* at ¶¶ 477-478. That compound is commercially available as Accolate®. *Id.* at ¶ 478.

B. ANALYSIS

1. Findings of Fact[4]

The Court finds the following facts to be true, having presided over a trial in this matter on February 23, 24, 25, and 26, 2009; having listened to and examined the testimony of Robert N. Young, Marc Labelle, and Gabriel Lopez, and experts Adam B. Jaffe, George R. Lenz, John G. Gleason, Christopher A. Vellturo, William L. Jorgensen, Eli O. Meltzer,[5] and having reviewed the deposition designations of Joseph Atkinson, Peter J. Barnes (De Bene Esse), Michel Belley, Jonathan Edelman, Marc Goshko, Daniel Guay, Serge Leger, Anne L. Payne, George Philip, Melody Richards, Patrick Roy, Jeffrey Snodgrass, Denise Allen Williams, Yi Bin Xiang, and Robert Zamboni, and having viewed all of the exhibits admitted into evidence.

a. Asthma and Allergic Rhinitis

Asthma is a chronic inflammatory disease that affects the lower airways of the lungs. (T. Tr., Feb. 25, 2009 P.M. 37:17-18 (Meltzer); TEX 3183.0002). Asthma can be triggered by a number of stimuli, including allergens, irritants such as tobacco smoke or pollutants, respiratory

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[4] To the extent that any of the findings of fact might constitute conclusions of law, they are adopted as such. Conversely, to the extent that any conclusions of law constitute findings of fact, they are adopted as such.

[5] It appears from the record that, although both parties have submitted evidence of their respective expert witnesses qualifications to be treated as such, neither party actually moved for leave to treat such witnesses' testimony as expert testimony pursuant to F.R.E. 702. Having reviewed these witnesses qualifications, the Court now concludes that each of these witnesses' testimony shall be considered expert testimony under F.R.E. 702.

infections, weather conditions, exercise, and even certain medications. *Id.* at 37:18-23. These stimuli cause the release of mediators and inflammatory cells, which then result in the physical symptoms associated with asthma. *Id.* at 37:23-38:11. The characteristic symptoms of asthma are bronchoconstriction, dyspnea (shortness of breath), cough, chest congestion, excessive production of mucus, hypersensitivity of the airways, swelling of the airways, and lung inflammation. *Id.* at 38:3-11; TEX 3183.0002. Asthma is characterized by class as either intermittent or persistent. (T. Tr., Feb. 25, 2009 P.M. 40:16-18 (Meltzer)). Within the persistent classification, asthma can be labeled as mild, moderate, or severe. *Id.* at 40:16-18. The actors which determine what class of asthma a particular person is suffering from include the frequency of the symptoms, the person's ability to physically perform all of their activities, whether the person requires a "rescue" inhaler for acute attacks, whether the person has normal lung function, and the frequency of exacerbations. *Id.* at 40:16-18.

Allergic rhinitis is a broad term that subsumes both seasonal allergic rhinitis and perennial allergic rhinitis. (Philip Dep. Tr. 58:18-23). Seasonal allergic rhinitis affects patients who are allergic to pollen (or other allergens) that is present in the spring or fall. *Id.* at 58:24-59:4. Perennial allergic rhinitis is related to a patient's allergies to substances that are present year-round and often found indoors and result in year-round symptoms. *Id.* at 59:5-9.

b. LTD_4 and LTD_4 Antagonists

In the 1930's and 1940's, scientists studying the lungs of guinea pigs discovered that a particular substance, which they called the slow reacting substance of anaphylaxis ("SRS-A"), produced in the guinea pigs' lungs caused the contraction of smooth muscle tissues in the lungs. (Revised Final Pretrial Order, Stipulated Fact 63). SRS-A comprises three leukotrienes: LTC4,

LTD_4, and LTE4. (TEX 0008.0004; T. Tr., Feb. 23, 2009 A.M. 45:3-5 (Young)). Leukotrienes, are substances that are produced in the lung and other organs and bind with receptors in the lung. *Id.* at 45:2-3. With both asthma and allergic rhinitis, the more severe the disease, the greater number of leukotrienes are present. (T. Tr., Feb. 25, 2009 P.M. 54:9-11 (Meltzer)).

LTD_4 is composed of a peptide and a lipid. (T. Tr., Feb. 23, 2009 A.M. 45:3-5 (Young)). The receptor that binds LTD_4 is the cysteinyl leukotriene receptor, or CysLT1 receptor, and is sometimes referred to as the LTD_4 receptor. (Revised Final Pretrial Order, Stipulated Facts 64, 65). LTD_4 is the most active leukotriene of the four types of known leukotrienes, which means that, on a weight-for-weight basis, it has the most potent activity in contracting muscles and stimulating the LTD_4 receptor. (TEX 0008.0004 (3158); T. Tr., Feb. 23, 2009 A.M. 45:15-17, 46:16-20 (Young)). When LTD_4 binds with the LTD_4 receptor, the muscles of the lungs contract, or spasm. (TEX 3283.0003). LTD_4 also stimulates the production of mucus and causes changes in vascular permeability, resulting in inflammation and swelling. *Id.*; T. Tr., Feb. 25, 2009 P.M. at 53:20-23 (Labelle).

An LTD_4 antagonist interacts with the receptor molecules in muscles and tissue, occupying the same site as the LTD_4 molecule would and prevents LTD_4 from interacting with the receptor, blocking the effects that LTD_4 has on muscle tissue. (T. Tr., Feb. 23, 2009 A.M. 47:10-15).

c. Merck's Efforts to Develop LTD_4 Antagonists

In 1979, Merck commenced a project relating to leukotrienes. (T. Tr., February 23, 2009 A.M. 42:4-9; 108:14-17 (Young)). In 1984, Dr. Robert Young, then an employee of Merck Frosst Canada, became responsible for managing Merck's Leukotriene program (the

"Leukotriene Program"). *Id.* at 90:1-5. Dr. Young led a group of four chemists during the early years of the Leukotriene Program, and eventually took full responsibility for the Leukotriene Program. *Id.* at 44:17-19. With ten to twelve scientists being involved in the Leukotriene Program at its inception, the Leukotriene Program grew over time, and eventually involved 20 some chemists and many biologists during the project's most active years. *Id.* at 48:1-4,15-18. The total number of people working on the project during the 1990-1991 time frame was between 40 and 45 just at Merck Frosst Canada. (T. Tr., Feb. 23, 2009 A.M. 132:4-7 (Labelle)).

The goal of the project was to create a compound that: (1) would antagonize the LTD_4 receptor in a potent manner, allowing for the compound to be administered in relatively low doses; (2) could be administered orally and would have a half-life allowing for once-a-day dosing; and (3) was safe, particularly because it would be used to treat a chronic disease – asthma – indefinitely. (T. Tr., Feb. 23, 2009 A.M. 49:14-50:2 (Young)).

At the beginning of the Leukotriene Program, LTD_4 served as a lead compound for some pharmaceutical development teams; in contrast, other teams, including Merck, started with the only known LTD_4 antagonist, FPL-55712. *Id.* at 50:7-11, 50:22-51:2. However, when Merck tested FPL-55712 (a known antagonist of SRS-A) it found that FPL-55712 had a very short half-life, was not well absorbed, and what was absorbed was rapidly metabolized. *Id.* at ¶ 85. Merck also searched for other potential lead compounds in its library, looking for compounds that might have a similar structure to FPL-55712. *Id.* at 51:5-8. Promising compounds would then be screened and tested in asthmatic rats. *Id.* at 52:24-53:1-8; 55:6-11, 55:20-22, 56:13-21.

1. L-648,051 and L-649,923

Of the compounds developed in the first few years of Merck's antagonist program, compounds, L-648,051 and L-649,923 were deemed to be potentially useful and went through multi-week and multi-month safety assessments, and then were finally formulated and brought to clinical trials. *Id.* at 58:5, 59:2-10. However, it was eventually determined that the amount of L-648,051 that was required to result in only a small reduction of bronchial constriction was too large, and the effect was not adequate. *Id.* at 62:14-18. Further, L-649,923 similarly did not show efficacy in treating asthma. *Id.* at 62:22-63:21. As such, both of these compounds were abandoned. *Id.* at 62:14-18, 62:22-63:21.

2. L-660,711 (MK-571)

The chemists next identified L-603,000 as a potential lead compound. *Id.* at 64:15-18. Due to L-603,000's simplicity and it's lack of an acidic group, the chemists made analogs of the compound by adding a chain with an acid of various lengths and found that doing so improved its activity. *Id.* at 65:15-21. They also found that adding a chlorine atom on the compounds' quinoline ring gave a boost of activity to it. *Id.* at 66:14-18. The Merck chemists eventually converted one of the two acid groups on L-603,000 to an amide, and made compounds containing a variety of amides. *Id.* at 67:12-15. The compound that showed the best results was L-660,711. *Id.* Pre-development data showed that L-660,711 was (1) very potent; (2) effective in animal studies; (3) well absorbed; and (4) had a good half-life. *Id.* at 67:20-23. Once accepted into development, L-660,711 was renamed MK-571 and clinical trials commenced in 1989. *Id.* at 65:22-66:7, 68:3-4. However, long term animal toxicity studies revealed liver side effects in rats. *Id.* at 68:19-23. Therefore, Merck abandoned MK-571. *Id.* at 69:1-4.

3. L-668,019 (MK-679)

The chemists then discovered that MK-571 was composed of two isomers: the R-isomer and the S-isomer. *Id.* at 69:13-15; Feb. 23, 2009 P.M. 19:5-9 (Labelle). It was further discovered that the R-isomer did not have the adverse liver effects seen in the MK-571 clinical trials. (T. Tr., Feb. 23, 2009 A.M. 70:2-4 (Young)). As such, the scientists isolated the R-isomer and prepared it as a separate compound, labeling it L-668,019, or MK-0679 and naming it verlukast. *Id.* at ¶ 124. This compound went to human clinical trials. *Id.* at 70:5-14. However, because liver effects were seen after long term human trials, Merck halted development of MK-679. *Id.* at ¶ 70:22-71:9.

4. L-669,392

In 1988, while MK-571 was moving to clinical trials, the goal of the Leukotriene Program shifted to the pursuit of a backup for MK-571 should there be a problem with MK-571 during clinical trials. (T. Tr., Feb. 23, 2009, P.M. 4:12-13, 4:16-21 (Labelle)). Using a trial and error approach, adopting changes that, after testing, showed beneficial properties, and then exploring additional options for further benefits. *Id.* at 49:12-17. The chemists began by changing the linker between the quinoline ring and the phenyl ring of MK-571. *Id.* at 5:6-12; 5:14-18. After trying a variety of different linkers, the scientists found that the resulting compounds were less potent, but still had good activity. *Id.*

The chemists then looked at the sulfur atom in the amide containing side chain of L-660,711 (the "Q^2"side chain) and replaced the sulfur with a carbon atom. *Id.* at 5:20-6:3. They found that this did not change the potency of the compound. *Id.* The chemists also recognized that the two side chains were interchangeable, and experimented with the amide on the Q^1 sulfur-containing side chain. *Id.* at 5:20-6:3.

The resulting compound was tested in animals and was found to have a short-half life and thus did not stay in the body long enough. *Id.* at 7:14-8:4, 8:17-24, 9:1-4. The chemists attempted to solve this issue by substituting different moieties in the alpha position on the Q^1 side chain and ran multiple assays to test each substitution and also by pulling metabolites from the blood of animal test subjects. *Id.* at 10:2-17, 10:21-11:4, 11:11-24; TEX 3183.0012-14. This lead the chemists to realize that amide functionality was undergoing metabolism, and so they would have to move away from using amides. *Id.*; T. Tr., Feb. 23, 2009 P.M. 11:11-24 (Labelle).

In order to avoid this amide problem, the chemists tried using about fifteen different amides in the compound; however, this did not solve the half-life problem. *Id.* at 15:21-25. After trying substituting various highly polar groups for the amides, including carboxylic acids, tetrazoles, sulfonamides and inverse sulfonamides, carbonates, and nitriles as well as less polar groups including sulfones, esthers, alcohols, ketones, oxides, isopropyl, and hydrogen. *Id.* at 15:21-25, 16:2-4, 16:9-21, 16:144-148).

The chemists eventually found that one group, a tertiary alcohol, worked quite well in solving the half-life problem. *Id.* at 20:3-10. Michel Belley made the compound containing the tertiary alcohol, L-691,054. *Id.* at 20:18-19, 21:2. However, L-691,054 also exhibited liver toxicity in initial testing. *Id.* at 21:2, 21:9-12. The chemists dealt with the toxicity problem by separating the compound into its four different isomers and found that the most potent isomers were also the most toxic. *Id.* at 22:2-10. The chemists focused on an isomer with less potency and less toxicity and after more testing and modifications to the compound found that the least toxic molecule contained a methyl ketone at the 12 o'clock position on the phenyl ring in the Q^2 position. *Id.* at 22:12-17, 25:15-27:14, 29:1-3, 29:14-21. The resulting

compound, L-669,392 was sent to development, and the chemists again began looking for another backup compound. *Id.* at 33:5-7.

5. Montelukast

In late 1990, the chemists returned to the tertiary alcohol series and again attempted to resolve the toxicity issues they confronted before. *Id.* at 33:18-34:9, 35:15-16. The chemists tried to modify the beta position of the tertiary alcohol containing molecules in an attempt to solve the toxicity issues. *Id.* at 35:3-8 . The Merck chemists first substituted one, then two, methyls in the beta position and found that the dimethyl substitution resulted in a compound with no enzyme induction and a longer half-life. *Id.* at 36:5-10 (Labelle); TEX 3183.0035. A carbon was then added to the Q^1 side chain and the resulting compound, L-705,254, had an even longer half-life and further reduced liver toxicity. (T. Tr., Feb. 23, 2009 P.M. 37:12-20 (Labelle); TEX 3183.0036).

The chemists then bonded the two methyls in the beta position to make a cyclopropyl ring and, after trying various analogs of this compound, found that the cyclopropyl-containing compound, L-706,631, was the most potent. (T. Tr., Feb. 23, 2009 P.M. 39:5-18 (Labelle); TEX 3183.0037). L-706,631 was re-named MK-476 in development, and proved to be (1) more potent than MK-679; (2) to have a longer half-life than MK-679; and (3) it did not cause liver toxicity. (T. Tr., Feb. 23, 2009 P.M. 40:12-22; TEX 3183.0038). The chemists recommended that MK-476 be considered for development. (Feb. 23, 2009, p.m., T. Tr. 40:23-41:7). MK-476 ultimately was re-named montelukast, the active ingredient in Singulair® tablets. (T. Tr., Feb. 23, 2009 P.M. 40:7-9 (Labelle); Revised Final Pretrial Order, Stipulated Fact 68). The chemical structure of montelukast is set forth in Figure 1, attached hereto in Appendix A.

d. The '473 Patent

The '473 patent is the sole patent in suit. (Revised Final Pretrial Order, Stipulated Fact 23). The named inventors of the '473 patent are Michel Belley, Dr. Serge Leger, Dr. Marc Labelle, Dr. Patrick Roy, Dr. Yi B. Xiang, and Dr. Daniel Guay. (Revised Final Pretrial Order, Stipulated Fact 24; TEX 3001).

Claims 18-22 of the '473 patent cover montelukast sodium, which is the active ingredient in the Singulair® tablets, Merck's pharmaceutical product used for treating certain ailments, including asthma and allergic rhinitis. Specifically: (1) Claim 18 is directed to a specific compound, montelukast, or its pharmaceutically acceptable salts. (Revised Final Pretrial Order, Stipulated Fact 32). Claim 19 is directed to the sodium salt of montelukast. *Id.* at 33. Claim 20 is directed to a pharmaceutical composition comprising a pharmaceutical carrier and an effective amount of the compound of claim 18. *Id.* at 34. Claim 21 is directed to a method of preventing the action of leukotrienes in a mammal by administering an effective amount of the compound of claim 18. *Id.* at 35. Claim 22 is directed to a method of treating asthma in a mammal by administering to a mammal in need of such treatment a therapeutically effective amount of a compound of claim 18. *Id.* at 36. The U.S. Patent and Trademark Office ("PTO") issued the '473 patent on October 15, 1996 from U.S. Patent Application Serial No. 08/392,592 ("the '592 application"), which was filed on February 23, 1995. The '592 application is a continuation of U.S. Patent Application Serial No. 07/774,414 ("the '414 application"), filed October 10, 1991, which is a continuation-in-part of U.S. Patent Application Serial No. 07/741,888 ("the '888 application"), filed on August 8, 1991, which is a continuation-in-part of U.S. Patent Application Serial No. 07/596,877 ("the '887 application") filed on October 12, 1990. *Id.* at 26. Claims 18-

22 of the '473 patent, which cover montelukast, are entitled to a date of invention no earlier than August 8, 1991, the filing date of the '888 application. *Id.* at 104.

(1) The Prosecution History of the '473 Patent

The '887 application, filed on October 12, 1990, include compound claims, composition claims and method claims. *Id.* at 69-70. In an Office Action mailed on March 18, 1991, the examiner rejected the claims on various grounds, including as obvious in view of U.S. Patent No. 4,962,203 ("Young 203"). *Id.* at 71. In its Reply dated June 18, 1991, MSD distinguished the alleged invention from Young '203 stating that the compounds in Young '203 "differ significantly from the present invention in that the Q side chain is attached directly to the benzene ring by a heteroatom; whereas the present compounds have the Q side chains insulated from the benzene ring by a saturated carbon atom. Furthermore, the compounds in [Young '203] have one polar Q per side chain, whereas the present compounds have two such groups." *Id.* at 72. Further, in the same Reply, Mr. Lopez cited Young '093 and stated that "the present compounds differ from EP 318,093 in that Q^2 is a secondary or tertiary alcohol or amine." *Id.* at 73. In an Office Action mailed on October 8,1991, the examiner rejected the claims as anticipated by or, in the alternative, as obvious over Young '093, stating "Claims 1 to 9 are rejected under 35 U.S.C. § 102(a) and (b) as anticipated by or in the alternative under 35 U.S.C. § 103 as obvious over [Young '093]. Patentee' [*sic*] all teach the compound claims as well as comparable scope." *Id*. at 74. MSD did not respond to this objection and on May 19, 1992, a Notice of Abandonment of the '887 application was issued. *Id.* at 75-76.

On August 8, 1991, the '888 application was filed. *Id.* at 79. Montelukast was disclosed in the '888 application as Example 161. *Id*. at 80. In an Office Action mailed on April, 9, 1992,

the examiner rejected the claims as anticipated by or, in the alternative, as obvious over Young '093, stating the same grounds for rejection as those stated in the October 8, 1991 rejection action on the '887 application. *Id*. at 81. Again, MSD did not respond to this objection and on December 17, 1992, a Notice of Abandonment of the '888 application was issued. *Id.* at 82-83.

The '414 application was filed on October 10, 1991. *Id.* at 84. On May 4, 1992, MSD submitted an Information Disclosure Statement listing references including Young '409 and European Patent EP 0 399 818 ("Young '818"). *Id.* at 87. The examiner rejected the claims as anticipated or obvious based on Young '409, stating in an Office Action dated May 26, 1992, that "Patentees' all teach the claimed quinoline derivatives" and that Young '409 disclosed examples where "Q2 is CH2-OH and Y = -CH=CH," and so disclosed compounds where Q^2 could be a primary alcohol. *Id.* at 88. In a Reply and Amendment dated August 26, 1992, Mr. Lopez traversed the rejection on this ground, stating that "[t]he present definitions of Z^1/Z^2 = $CONR^3$. Any one of these differences would render the present compounds unobvious; the combination of three substantial differences appears irrefutable." *Id* at 89. On December 15, 1992, the examiner issued an office action without repeating the rejection based on Young '409 and a Notice of Allowance was issued on November 28, 1994. *Id.* at 90-91. However, on December 19, 1995 a Notice of Abandonment was issued for MSD's failure to timely pay the issue fee. *Id.* at 92. On February 23, 1995, the '592 application was filed and a Notice of Allowance was issued on April 16, 1996. *Id* at 93-94. The '473 patent issued on October 15, 1996.

On February 20, 1998, the FDA approved the use of Singulair® tablets in 10 mg form and 5 mg form for the prophylaxis and chronic treatment of asthma in patients 15 years of age and

older and pediatric patients from 6 to 14 years of age, respectively. *Id.* at 42. The FDA subsequently approved various other dosages and forms and for the treatment of perennial and seasonal allergic rhinitis as well as for the prevention of exercise-induced bronchoconstriction ("EIB"). *Id.* at 44-47.

e. Teva's Abbreviated New Drug Applications

Teva filed ANDA No. 78-605 with the FDA a paragraph III certification pursuant to 21 U.S.C. § 355(j)(2) on November 13, 2006, seeking approval for generic tablets containing 10 mg of montelukast sodium. *Id.* at 55. On December 22, 2006, Teva USA filed ANDA No. 78-723 as a paragraph III certification pursuant to 21 U.S.C. § 355(j)(2) for generic tablet containing 4 mg and 5 mg of montelukast sodium. *Id*. at 58; TEX 3004.0001, 0020. No later than February 23, 2007, MSD received notice that Teva revised ANDA No. 78-605 to include a Paragraph IV certification under 21 U.S.C. § 355(j)(2)(A)(vii). (Revised Final Pretrial Order, Stipulated Facts 5, 7). Similarly, on or about April 2, 2007 MSD received similar notice that Teva had also revised ANDA No. 78-723 to include a Paragraph IV certification under 21 U.S.C. § 355(j)(2)(A)(vii). *Id*. at 15.

Teva admits that the montelukast sodium tablets that are the subject of its ANDA Nos. 78-605 and 78-723 infringe claims 1, 7, and 18-22 of the '473 patent if those claims are upheld as valid and enforceable. (Revised Final Pretrial Order, Stipulated Fact 37). However, as discussed in greater detail below, pursuant to a stipulation entered on February 23, 2009, MSD agreed to dismiss with prejudice its claim of infringement of claims 1 and 7 of the '473 patent. [Docket No. 93].

f. Procedural History

On April 3, 2007, MSD filed a complaint in the United States District Court for the District of New Jersey, Civil Action No. 07-1596 (GEB), alleging infringement of the '473 patent under 35 U.S.C. § 271(e)(2)(A) by Teva USA, based on Teva USA's ANDA No. 78-605 filing, and aiding and abetting infringement by Teva Ltd. *Id.* at 8. Pursuant to Title 21, United States Code § 355(j)(5)(B)(iii), the filing of Merck's complaint stayed the potential FDA approval of Teva's ANDA No. 78- 605 for thirty months from the date that Merck received notice that Teva USA filed ANDA No. 78-605. *Id.* at 9. The thirty month stay on the potential FDA approval of Teva's ANDA No. 78-605 expires on or about August 23, 2009. *Id.* at 10. On May 29, 2007, Defendants filed their Answer, Affirmative Defenses, and Counterclaims to MSD's complaint. *Id.* at 11. On June 18, 2007, Merck entered its Reply to the Counterclaims of Teva related to Merck's complaint based on Teva's filing of ANDA No. 78-605. *Id.* at 11.

On May 14, 2007, MSD filed another complaint in the United States District Court for the District of New Jersey (Civil Action Number 07-2264 (GEB)), alleging infringement of the '473 patent under 35 U.S.C. § 271(e)(2)(A), based on Teva USA's ANDA No. 78-723 filing. *Id.* at 16. On June 12, 2007, Defendants filed their Answer, Affirmative Defenses, and Counterclaims to MSD's complaint based on Teva USA's ANDA No. 78-723. *Id.* at 17. On July 2, 2007, MSD entered its Reply to the Counterclaims of Defendants related to Teva's ANDA No. 07-723. *Id.* at 18.

MSD filed First Amended Complaints in both actions on August 6, 2007, regarding the alleged infringement of the '473 patent based on Defendant Teva's filing of ANDA Nos. 78-605 and 78-723. *Id.* at 19.

On August 7, 2007, the Court ordered the two cases, Civil Action Numbers 07-1596 and

07-2264, to be consolidated as Civil Action Number 07-1596 (GEB) for all purposes. *Id*. at 20.

Defendants filed their Answer to Amended Complaint and asserted Affirmative Defenses and Counterclaims to Merck's First Amended Complaint based on Teva's filing of ANDA No. 78-723 on August 17, 2007. *Id*. at 21. Subsequently, MSD filed its Replies to these Counterclaims on August 30, 2007. *Id*. at 22.

(1) Teva's Motion to Compel

On September 8, 2008, Teva filed a Motion to Compel, seeking an Order from the Court to compel MSD to produce "all allegedly privileged communications relating to MSD's failure to disclose highly material prior art during the prosecution of the patent-in-suit or alternatively, for an order that those involved in the prosecution of the '473 patent be precluded from testifying about their alleged good faith state of mind in connection with their failure to disclose this highly material prior art." (Teva's Mot. to Compel at 1 [Docket No. 32]). On November 5, 2008, United States Magistrate Judge John J. Hughes denied the Motion to Compel on the ground that the crime-fraud exception does not apply and alternatively because there was no waiver of attorney client privilege in the instant matter. (Mem. Op. at 11, 13 [Docket No. 41]). The alternative relief sought by Teva , specifically precluding MSD from offering alleged good faith explanations from those involved in the prosecution of the '473 patent for their non-disclosure of the [Young 89 Model], was also denied as moot because "MSD's outside counsel found no responsive privileged documents in Merck's privileged documents log." *Id.* at 15.

(2) The Parties' Motions in Limine and Pretrial Briefs

Shortly before the commencement of trial, the parties filed several motions in limine with respect to certain evidentiary disputes. On February 5, 2009, MSD filed its Deceptive Intent

Motion, seeking to preclude Teva from offering evidence of deceptive intent in support of the inequitable conduct claim related to the prosecution of the '473 patent. [Docket No. 64]. MSD argued that Teva previously made this argument in its Motion to Compel before Judge Hughes and because Teva had chosen not to appeal Judge Hughes' November 5, 2008 Memorandum Opinion and Order denying Teva's motion, Judge Hughes' ruling had now become the law of the case. *Id.* at 2. On February 20, 2009 an Order was entered with respect to MSD's Deceptive Intent Motion, holding that "decision is reserved on plaintiff's motion that Teva be barred from presenting any evidence as to deceptive intent , without prejudice to reassertion of the motion at conclusion of trial." [Docket No. 85].

On February 11, 2009, MSD filed additional Motions in Limine, seeking to preclude Teva from offering: "(i) evidence of art that Teva claims is prior art to [the '473 patent] under 35 U.S.C. § 102(e), (ii) expert testimony from Dr. Adam B. Jaffe regarding unsupported allegations that scientific articles addressing the safety and efficacy of MSD's Singulair® tablets were ghostwritten, and (iii) expert testimony from Dr. Jaffe regarding evidence pertaining to Neurontin® and Nesiritide product, which are not part of this case." (MSD's Mots. in Limine at 1 [Docket No. 70-2]). On February 20, 2009, the Court entered an Order: (1) denying without prejudice MSD's motion that Teva be barred from presenting evidence of prior art under 35 U.S.C. § 102(e); (2) reserving its decision on MSD's motion that Teva be barred from presenting certain of Dr. Jaffe's expert testimony regarding the ghostwriting of scientific articles explaining the safety and efficacy of Singulair®; and (3) reserving its decision on MSD's motion that Teva be barred from presenting certain of Dr. Jaffe's expert testimony regarding evidence pertaining to Neurotonin® and Nesiritide products. [Docket No. 101].

MSD filed another motion in limine on February 11, 2009, seeking to limit the testimony of Teva's expert witness, Dr. George R. Lenz ("MSD's Lenz Motion"). [Docket No. 84]. Here, MSD sought to preclude Teva from offering evidence "that a person having ordinary skill in the art would have identified compound 97 of the '882 patent as the 'one and only' lead compound most promising to modify in order to develop a safe and effective leukotriene antagonist." (MSD's Lenz Mot. at 2). On February 20, 2009, the Court denied this motion without prejudice. [Docket No. 86].

Also on February 11, 2009, Teva filed a motion in limine to preclude MSD's evidence of unexpected results in the development of the compound montelukast ("Teva's Unexpected Results Motion"). [Docket No. 71]. On February 20, 2009, the Court denied this motion without prejudice. [Docket No. 87]. Both parties also filed their pretrial briefs on February 11, 2009. (MSD's Pretrial Br. [Docket No. 70]; Teva's Pretrial Br. [Docket No. 74]).

(3) Stipulation Limiting Issues at Trial

The parties entered into a stipulation agreeing to certain limitations on the issues presented at trial ("Stipulation"), which this Court so ordered on February 23, 2009. (Stipulation [Docket No. 93]). In the Stipulation, MSD agreed to dismiss with prejudice its claim of infringement of claims 1 and 7 of the '473 patent. *Id*. Teva agreed that they would not rely upon U.S. Patent Nos. 5,428,033 and 5,266,568 and the disclosure of their respective applications as prior art under 35 U.S.C. § 102(e) to any of the claims of the '473 patent for the purpose of the trial. *Id*.

(4) Trial and Post-Trial Submissions

The Court conducted a four day non-jury trial from February 23 to 26, 2009. (Trial

Transcripts [Docket Nos. 91, 94-95, 97-98, 100, 105]). Subsequently, the parties submitted findings of fact and conclusions of law. (Teva's Proposed Stmt. of Facts [Docket Nos. 111 (sealed version) and 114 (public version)]; MSD's Proposed Stmt. of Facts [Docket No. 115]; Jt. Stmt. of Law Regarding Inequitable Conduct [Docket No. 112]; Jt. Stmt. of Facts Regarding Obviousness [Docket No. 113].

(5) The PTO's Reexamination of the '473 Patent

On May 28, 2009, Teva filed a letter, alerting the Court that, on May 20, 2009, the PTO granted an ex parte request for reexamination of the '473 patent. [Docket No. 118]. In granting reexamination, the PTO determined that several references that were not presented during the prosecution of the '473 Patent, including Young 89, raised a substantial new issue of patentability. (PTO Order Granting Reexamination, attached to Teva's Letter, at ¶¶ 9-10 (stating Young 89 "raises a substantial new question of patentability as to claims 1, 7, 18-22.")) Teva argues that the decision by the PTO to reexamine the '473 patent is relevant to the its defense of inequitable conduct because the PTO's grant of the request for reexamination supports Teva's position that Young 89 is material. *Id.* at 2.

On June 1, 2009, MSD filed a response, arguing that the PTO's decision to reexamine the '473 patent is not relevant in the current case because: (1) the PTO almost always finds a substantial new question of patentability and therefore initiates a reexamination; and (2) the PTO is required to apply less stringent standards in determining whether to grant reexamination than than those which this Court is required to apply in its review of the '473 Patent. (MSD's Letter at 1 [Docket No. 119]).

g. The Parties' Definitions of a Person of Ordinary Skill in the Art and Dr. Lenz's and Dr. Gleason's Qualifications

The Court finds that Teva's paragraph IV certification notice included the following definition of the level of skill in the art:

> The prior art demonstrates a reasonably high level of skill. One of ordinary skill in the art would possess substantial training in chemical and biological sciences with a Ph.D. or equivalent degree, training in the areas of synthetic organic chemistry, pharmacology or a related field, and experience working in research and development of leukotriene antagonists and leukotriene biosynthesis inhibitors. This person would have familiarity with the classes of leukotrienes, structure/function relationships of small molecule binding to the leukotriene receptors as well as standard assays in the art for determining in vivo activity as both leukotriene antagonists or leukotriene biosynthesis inhibitors. Such an individual would easily have understood the prior art references and have the capacity to draw inferences from them.

(TEX 3005.0006-0007). The Court finds that, after hiring Dr. Lenz to conduct Teva's obviousness analysis, Teva submitted a new definition of one of ordinary skill in the art in the Revised Final Pretrial Order, which omits any reference to a person of ordinary skill in the art having experience in the art of designing leukotriene antagonists:

> As of October 12, 1990, the hypothetical person having ordinary skill in the art of the '473 patent would possess a reasonably high level of skill. One having ordinary skill in the art would possess substantial training and experience in medicinal chemistry, experience or training in the chemical and biological sciences with a Ph.D. or equivalent degree in chemistry, experience or training in synthetic organic chemistry, and at least two years of experience in drug discovery, design, testing, and development. Such a person would have understood the prior art references and have the capacity to draw inferences from them, individually and overall, in designing LTD_4 antagonists.

(Revised Final Pretrial Order at 54, ¶ 98 [Docket No. 62]). MSD also submitted its own definition of a person of ordinary skill in the art as a part of the Revised Final Pretrial Order:

> One of ordinary skill in the art should be understood as someone with substantial training in the chemical and biological sciences

> with an advanced degree in chemistry, training in the areas of synthetic organic chemistry and medicinal chemistry, and substantial experience working in the research and development of leukotriene antagonists.

Id. at 24, ¶ 99.

The Court finds that Dr. John G. Gleason, Merck's medicinal chemistry expert, received a bachelor's degree in Chemistry from Loyola and a PhD in Chemistry from McGill University. (T. Tr., Feb. 25, 2009 A.M. 41:10-13 (Gleason)). Dr. Gleason then completed a year-long post doctoral fellowship at the Swiss Federal Institute of Technology in Zurich before joining SK&F in 1971 as a medicinal chemist, where he worked for about 37 years before retiring. *Id.* at 41:13-16; 17-20. During his employment, Dr. Gleason served as Vice President and Director of Medicinal Chemistry for United States operations and Vice President of Chemistry for the Cardiovascular Urogenital and Oncology Center of Excellence for Drug Discovery after the merger. The Court also finds that Dr. Gleason was involved in SK&F's LTD_4 antagonist program since before the discovery of the leukotrienes. *Id.* at 42:17-21. Dr. Gleason was one of the originators of SK&F's leukotriene antagonist development program and led the chemistry side of that program as either Program Leader or Co-Leader for its entire duration which lasted from late-1979/early-1980 through the early 1990s. *Id.* at 43:3-15. Further, Dr. Gleason attended several conferences on leukotriene antagonist development and was invited as a speaker to many of them as well. *Id.* at 45:22-46:1.

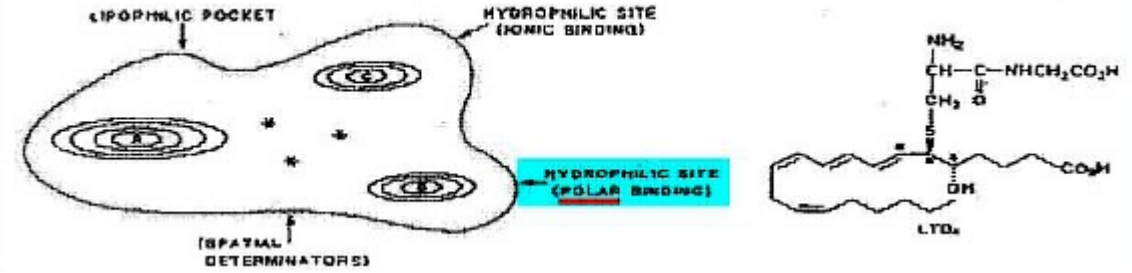
The Court finds that Dr. George R. Lenz, Teva's medicinal chemistry expert, received a bachelor's degree in Chemistry from the Illinois Institute of Technology master of science and a Ph.D., both in physical sciences from the University of Chicago. (T. Tr., Feb. 24, 2009 A.M. 74:21-75:7 (Lenz). However, Dr. Lenz never worked in the field of LTD_4 antagonists. *Id.* at

136:3-5. In order to educate himself in that field Dr. Lenz read approximately 50 articles before rendering his opinion, some of which were published after the 1990 to 1991 timeframe. *Id.* at 138:10-15, 138:16-139:3. Further the Court finds credible Dr. Lenz's testimony that the a chapter titled "Leukotriene Receptors," appearing in *Comprehensive Medicinal Chemistry* and written by W. Kingsbury and others, including Dr. Gleason ("the Kingsbury publication"), sets out the state of the art in 1990 for leukotriene antagonist development fairly accurately. *Id.* at 140:17-23; 142:10-14; TEX 3131). The Court Court finds that Dr. Lenz did not attend any conferences or meetings related to leukotriene antagonists and did not speak to anyone who had attended such meetings. (T. Tr., Feb. 24, 2009 A.M. 140:17-23; 142:10-14 (Lenz)). The Court additionally finds that for at least the last 14 months, Dr. Lenz has worked mostly as a consultant in litigations, not a medicinal chemist. *Id.* at 18:19-25.

h. The Young 89 Model

The Court finds that Dr. Young, while employed at Merck Frosst Canada and while working on Merck's Leukotriene Program, presented the Young 89 Model, which is depicted as follows, at a conference in Taipei:

the region of the 7,8 double bond. 2) The binding of the cysteinyl-glycine unit likely involves both hydrogen bond and ionic interactions and the acid is probably ionized in the receptor. These postulates are supported by evidence that the conversion of the glycine acid to an amide or cyclic diketopiperazine leads to a ten-fold loss in activity.[3] 3) The C-1 carboxyl group binds through H-bonds and is likely not ionized in the receptor (as the primary amide analog is equipotent). 4) The C-5 hydroxyl group binds to the receptor sufficiently strongly to impart stereospecific recognition of both the relative and absolute stereochemistry at C-5 and C-6 of LTD_4.



(T. Tr., Feb. 23, 2009 A.M. 71:22-72:3, 73:12-20; PTX 3283 at 3283.0002 (emphasis provided by Teva)). Following the Taipei conference, Dr. Young published Young 89, which summarized his presentation and which included the Young 89 Model (PTX 3283). Thus, as of 1989, Young 89 was available to the public, including Merck's competitors. The Court further finds that neither Young 89, nor the Young 89 Model, were ever submitted to the PTO during the prosecution that resulted in the '473 patent. (Revised Final Pretrial Order, Stipulated Fact 121).

The Young 89 Model identifies three attributes that the group located at the "B" pocket of the receptor in the model must have: it must be: (1) polar; (2) not ionized; and (3) a hydrogen bond acceptor. (T. Tr. Feb. 24, 2009, A.M. 119:23-120:2; 121:16-122:4 (Lenz); PTX3283 at 3283.0002; T. Tr. Feb. 23, 2009, A.M. 98:10-99:19 (Young)). However, the Young 89 Model does not address many other factors such as: (1) the steric requirements; (2) the shape of the receptor; (3) the requisite polarity to bind with the receptor; (4) and the directionality of potential

hydrogen bonds. (T. Tr., Feb. 25, 2009 A.M. 107:11-15, 107:23-108:4, (Gleason)). As such, the Young 89 Model is very broad and does not provide significant guidance as to how to distinguish between the many number of potential compounds that fit the model. (T. Tr., Feb. 25, 2009 A.M. 66:1-4; 72:5-9, (Gleason)). Indeed the Court finds persuasive the testimony of Dr. Young and Dr. Gleason that "many millions" and "hundreds of thousands, millions" of compounds could fit within the bounds of the Young 89 Model. (T. Tr., Feb. 23, 2009 A.M. 76:2-7, (Young); T. Tr., Feb. 25, 2009 A.M. 66:1-4, (Gleason)).

The Court further finds that Young 89 does not definitively suggest the use of a tertiary alcohol in the Q^2 position of a proposed LTD_4 antagonist. (Belley Dep. Tr. 33:3-34:3). The Court notes that Defendants' expert witness, Dr. Lenz, testified that a medicinal chemist would use various tools to create a hierarchy of compatible substituents and a tertiary alcohol would be at, or near, the top of the list of substituents to use at the Q^2 side chain even though other groups fit the Young 89 Model. (T. Tr. Feb. 24, 2009, A.M. 131: 22-132:14, (Lenz)). Additionally, the Court notes that Mr. Belley testified that he first came up with the idea of using a tertiary alcohol in the Q^2 side chain after a meeting in which Dr. Young presented the Young 89 Model to him. (Belley Dep. 34:16-35:13). However, the Court finds compelling that Mr. Belley also testified, when asked whether montelukast fits the Young 89 Model, that

> "[w]hen the model was developed by Bob Young and Bob Zamboni, when I suggested to put a tertiary alcohol there, they said it's not going to work. . . . [A]ccording to the reaction, the answer would be no. But I probably would have argued the other way around. So the answer is not a definitive yes or a definitive no. You are in a gray zone there. . . because the alcohol is not the same polarity as an acid or an amide, and it's also not the same kind of hydrogen bond or donor receptor. It's weaker. So chances are it could be active or could be not active. You don't know."

Id at 68:23-69:15. Further, the Court also finds credible several of MSD's witnesses who testified that a tertiary alcohol is a surprising choice for the Q^2 side chain. For example, Dr. Young testified that he did not believe a tertiary alcohol would be a good choice. (T. Tr., 2/23/2009 A.M. 79:15-80:2, (Young). Dr. Jorgensen also stated that "[t]ertiary alcohols, particularly benzylic or allylic, are unstable and are expected to decompose in even mildly acidic conditions. So it is very unusual to see a tertiary alcohol on a drug." (T. Tr., 2/26/2009 29:20-23, (Jorgensen)). Further, Mr. Belley testified that, after he synthesized a compound containing a tertiary alcohol, "everybody was surprised to see its activity. They were surprised because it was active. They were surprised because it was more active than everything else at the time, and later there were surprised because it had good pharmacokinetics." (Belley Dep. Tr. 37:7-15, 54:18-24; *see also* Guay Dep. Tr. 47:2-4 ("[S]omeone had made a tertiary alcohol compound, and it had a very surprising and beneficial effect on the [pharmacokinetic] profile."); Zamboni Dep. Tr. 35:17-21.)

The Court also finds that the Young 89 Model does not suggest that a tertiary alcohol would be interchangeable with a dimethyl amide. The Court finds compelling Dr. Young's testimony that although tertiary alcohols and dimethyl amides are moderately similar in size, with the tertiary alcohol being slightly smaller on a gross scale, the two substituents have different shapes, especially in the area where you would expect hydrogen binding to occur, and that "the size [of the two substituents] relative to the binding point . . . not the gross overall bulk" is the important difference. (T. Tr., Feb. 23, 2009 A.M. 118:14-119:2 (Young)).

The Court further finds credible Dr. Young's testimony that, when Mr. Belley suggested to Dr. Young that a tertiary alcohol be supplemented in place of an amide, he told Mr. Belley that

"he was wasting his time" because "[i]t was much too lipophilic an element" and as such the resulting molecule would not be potent. *Id.* at 79:15-80:2. Additionally, the Court finds credible the testimony of Dr. Jorgensen, a Merck expert witness, that the Young 89 Model does not teach anything about the interchangeability of a dimethyl amide and a tertiary alcohol. (T. Tr. Feb. 26, 2009 29:2-4).

The Court also finds compelling Dr. Lenz's testimony that the Young 89 Model does not teach whether the Q^1 side chain must terminate in a carboxylic acid. (T. Tr., Feb. 24, 2009 P.M. 18:15-17, 19:8-11, 28:20-24; 30:12-16 (Lenz)).

i. Teva's Lead Structure

The Court finds that by April of 1991, there existed at least ten compounds in the area of leukotriene antagonists that were in preclinical or clinical evaluations. (T. Tr., Feb. 24, 2009 P.M. 13:24-14:11; 33:17-34:3 (Lenz)). There were also biological assay data available for each of those ten compounds. *Id*. at 14:12-14, 14:17-18, 34:1-3. The Court also finds that five of those ten compounds are quinoline-based. *Id*. at 34:4-5; 42:14-20. The Court further finds that, during the relevant time period, there would have been no way to know which of the ten compounds in preclinical or clinical evaluations would eventually lead to a viable commercial compound. *Id* at 36:4-5, 18-23; T. Tr., Feb. 25, 2009 A.M. 64:5-11, 81:23-82:1, (Gleason).

The Court finds that the lead structure chosen by Teva is not an actual compound, but a concept for a compound. T. Tr., Feb. 24, 2009 P.M. 14:19-22 (Lenz). The Court finds that Teva has offered no explanation as to why a person of ordinary skill in the art would not have chosen one of the actual compounds over Teva's lead structure.

The Court finds credible Dr. Lenz's testimony that he applied four filters to come up

with his lead compound structure, found that compound 97 would have been particularly preferred because of the dimethyl amide at the "X" position of his generic lead structure, and that he looked to the '882 patent to see if there were any other compounds that satisfied his filters. *Id.* at 46:3-5, 49:5-7, 128:21-129:9, 46:14-17. The Court also finds that compounds 402, 409, 410, and 420 of the '882 patent also satisfy his four filters, even when the preferred and more restrictive criteria that "X" be a dimethyl amide is applied. *Id.* at 48:11-13, 49:16-18, 49:22-50:3, 50:14-16.

The Court finds that Teva's analysis requires at least eleven distinct steps from L-660,711 to Teva's lead structure to compound 97 to montelukast, of which is accomplished without the benefit or support of any biological data: In order to arrive at Teva's lead structure from L-660,711, one must :

1. Add a phenyl group to the Q^2 side chain. T. Tr., Feb. 25, 2009 A.M. 9:2-5, 9-14 (Lenz);
2. add a substituent "X" to the phenyl ring on the Q^2 side chain and chose where to attach the "X" substituent (ortho, meta, or para positions possible. *Id*. at 9:15-10:7;
3. replace the sulfur atom of one of the two side chains with a carbon and chose to do so in the Q^2 side chain. *Id*. at 10:8-10, 12:21-13:7, 13:12-19;

Then, in order to arrive at compound 97, one must:

4. choose a dimethyl amide for the "X" position of Teva's lead structure. *Id*. at 15:7-10;

In order to arrive at montelukast from this point, one must then:

5. choose to modify compound 97 by replacing the dimethyl amide, despite the fact that one chose dimethyl amide in the first place because L-660,711 showed it worked well. *Id*. at 15:11-21;

6. choose an alcohol to replace the dimethyl amide and then chose tertiary alcohols from among at least three different types of alcohols. *Id*. at 16:18-25;

7. choose to lengthen the Q^1 side chain (but not experiment with the length of the Q^2 side chain) by a single carbon (as opposed to shorten or lengthen by more than one carbon). *Id*. at 17:1-7;

8. choose to add a group to the Q^1 side chain. *Id*. at 17: 8-10;

9. choose what position (alpha or beta) to add the group and chose to add two methyl groups to that position. *Id*. at 17:11-14;

10. choose to convert those two methyl groups to a cyclopropyl group. *Id*. at 17:15-18:21; and

11. resolve the racemate. *Id.* at 18:9-14.

The Court finds that Teva has not provided a sufficient basis to explain why the foregoing steps logically follow one another.

(1) Teva's Steps 1-3

The Court finds that Teva does not provide convincing evidence to explain why the Q^2 side chain should contain a phenyl ring. Dr. Lenz rationalizes the inclusion of a phenyl in the Q^2 side chain by saying that the '882 patent and Young '093 include such a structure. (T. Tr. Feb.

24, 2009 P.M.44:22-45:2, (Lenz)). However, Dr. Lenz cannot point to any support suggesting that the inclusion of a phenyl ring in the Q^2 side chain would result in increased activity or other desirable properties. Further, Dr. Lenz's assertion is belied by Dr. Gleason's testimony that he could not see any reason to impose the inclusion of a phenyl ring in the Q^2 side chain as a filter for the lead compound structure, because there is no data or suggestion in the literature that doing so would be an effective modification. (T. Tr. Feb. 25, 2009 A.M. at 91:21-92:2, (Gleason)).

(2) Teva's Steps 4-7

Further, as noted above, the Court finds that the Young 89 Model does not teach that a primary alcohol would be interchangeable with either a secondary or a tertiary alcohol. (T. Tr., Feb. 23, 2009 A.M. 79:15-80:2, 83:8-14 (Young); T. Tr., Feb. 26, 2009 29:2-4, 29:20-23, 30:2-4 (Jorgensen); Tr., Feb. 25, 2009 A.M. 49:25-50:50, (Gleason); Belley Dep. Tr. 33:3-34:3).

The Court also finds that Teva does not provide convincing support for Dr. Lenz's decision to lengthen the Q^1 side chain. At the time the invention was made, the only literature that provided some guidance as to whether the Q^1 side chain should be lengthened is the Perchonock Paper. (TEX 3143; T. Tr., Feb. 24, 2009 P.M. 70:3-10, (Lenz); T. Tr. Feb. 25, 2009 A.M. 95:20-25, (Gleason)). Dr. Lenz admitted that the Perchonock Paper revealed undesirable result when the SK&F scientists increased the length of the side chain corresponding to the Q^1 side chain to three carbons-"[j]ust like the side chain in [Dr. Lenz's] lead structure." (T. Tr. Feb. 24. 2009 P.M. 70:15-22, 71:13-15, (Lenz)).

(3) Teva's Steps 8-11

Further, the Court also finds that Teva does not provide convincing support for Dr. Lenz's assertion that beta-oxidation of the Q^1 side chain was a concern. Dr. Lenz testified that a

person of ordinary skill in the art would have been concerned about beta-oxidation of the Q^1 side chain and that this concern would have led that person to add substituents to the beta-position of the Q^1 side chain to block the oxidation. (T. Tr., Feb. 24, 2009 AM. 130:1-16, 130:25-131:6, (Lenz)). However, Merck cited two papers to show that a Person of ordinary skill in the art would not have been concerned with beta-oxidation: (1) the Newton Paper, and (2) the Hay Paper. (TEX 3360; TEX 3141; T. Tr., Feb. 24, 2009 P.M. 73:16-24, 76:1-7, 76:25-77:2, (Lenz)). The Court finds this evidence more compelling than Dr. Lenz's testimony to the contrary.

Teva further argues that Dr. Leger, a named inventor of the '473 patent, admitted that one metabolic issue he dealt with was oxidation on the side chains and that his first approach in trying to prevent such oxidation was to add substitutions such as methyl or dimethyls, to the side chain. (Leger Dep. 84:14-85:7). Leger, however, did not specifically address beta-oxidation on the Q^1 side chain. In addition, the Court finds compelling Dr. Gleason's testimony that a person of ordinary skill in the art would not have been motivated in 1990 to 1991 to make a substitution in the beta position of the Q^1 side chain because there was no suggestion that there was significant metabolism taking place. (T. Tr., Feb. 25, 2009 A.M. 96:6-8, 96:12-18, 96:21-97:10, 97:24-25, (Gleason)). Moreover, the Court also finds compelling the testimony of Dr. Gleason that "in this timeframe, 1990, cyclopropyl groups were not easy to make" and that "[c]yclopropyl is not that commonly used." *Id.* at 100:10-19. The Court also finds compelling Dr. Gleason's assertion that inserting two methyl groups instead of cyclopropyl would be just as effective as stopping the beta-oxidation and would also be far easier to do. *Id.* Therefore, the Court finds that, even if a person of ordinary skill in the art would have been concerned about beta-oxidation, they would not have been motivated to include a cyclopropyl substituent at the beta-position of

the Q^1 side chain.

j. The Prosecution History of the '473 Patent

The Court finds that Mr. Lopez was employed by Merck as a patent attorney from approximately 1977 to 1993 and that during his period of employment, he wrote and prosecuted several patent applications, including the patents to which the '473 patent claims priority, but that he did not file or prosecute the '473 patent. (T. Tr., Feb. 24, 2009 A.M. 6:12-25, 7:1-7, 46:1-18 (Lopez)). The Court also finds that, during the 1990 through 1993 time frame, Mr. Lopez was generally aware that the Merck scientists working in the Leukotriene Program would try to understand how to construct a receptor antagonist through the use of models and that receptors typically have three or more points of contact. (T. Tr., Feb. 24, 2009 A.M. 42:23-43:2; 43:23-44:13 (Lopez)).

In the Reply to the patent examiner's rejection of the '414 application as obvious over Young '409, Mr. Lopez stated that "'[t]he present compounds differ from the art in that Q^2 is a secondary or tertiary alcohol or amine and that the present Z1/Z2 = CONR3. Any one of these differences would render the present compounds unobvious; the combination of three substantial differences appears irrefutable.'" TEX 1444.0609. The Court finds that this statement is consistent with the testimony of several of Merck's witnesses as well as the testimony of Teva's expert, Dr. Lenz. For example, Dr. Jorgensen testified that "[t]here isn't any interchangeability . . . between primary, secondary, and tertiary alcohols. They're very different beasts." (T. Tr., Feb. 26, 2009 30:2-4, (Jorgensen)). Dr. Young also testified that a tertiary alcohol is not interchangeable with a primary alcohol. (T. Tr., Feb. 23, 2009, A.M. 83:8-14, (Young)). Further Dr. Lenz testified that there are differences between primary alcohols and secondary or tertiary

alcohols, such as their chemical and metabolic properties. (T. Tr., Feb. 24, 2009 A.M. 114:12-115:6 (Lenz)).

The Court finds that during the time frame that Mr. Lopez was employed at Merck, there was a procedure in place by which materials that were proposed to be released to the public first had to be approved by certain individuals and Mr. Lopez was one of the reviewers. (T. Tr., 2/24/2009 A.M. 10:21- 11:21, (Lopez)). The Court finds credible Mr. Lopez's testimony that as a part of that procedure, he reviewed 100 or so manuscript approvals on an annual basis and that such reviews made up only a small portion of his job responsibilities. *Id.* at 60:7-15. The Court also finds that, as a result of this large number of manuscript approvals he was required to review, Mr. Lopez read less of a proposed manuscript if there were indications that suggested to him that approval of the manuscript would not be problematic and that factors that would influence Mr. Lopez's decision regarding how much time we would spend reviewing a manuscript include whether: (1) the author, especially an author that Mr. Lopez trusted, indicated that there was nothing in the manuscript that had not been approved before; (2) a patent had been issued regarding the subject matter of the manuscript; or (3) a patent application had been filed regarding the subject matter of the manuscript. *Id.* at 60:7-15, 60:16-61:3, 61:13-25.

Two years before the filing date of the '887 application, the earliest continuation-in-part to which the '473 patent claims priority, Mr. Lopez approved for release a manuscript of what was eventually published as Young 89. (TEX 1410; Stipulated Fact 26). The manuscript indicates that multiple patent applications already had been filed covering the subject matter of this manuscript. (TEX 1410.0002). However, despite this fact, the manuscript includes Mr. Lopez's handwritten note stating that this assertion is incorrect and reading "NO – 1290 was an

abstract only," which indicates that Mr. Lopez reviewed this manuscript in its entirety. (T. Tr., Feb. 24, 2009 A.M. 70:11-22; TEX 1410 at MSD02113350). Nevertheless, the Court finds credible Mr. Lopez's assertion that he does not recall the line of inquiry that led him to conclude that all of the information in this manuscript had not been previously cleared. (T. Tr., Feb. 24, 2009 A.M. 70:11-71:18 (Lopez)).

Mr. Lopez also reviewed several other manuscripts that contained references to the Young 89 Model. *Id*. at 12:18-41:25; DTX 1207, DTX 1411, DTX 1285, DTX 104, DTX 105, DTX 1467, DTX 1263, DTX 1465, DTX 1227. However, several of these manuscripts do not identify the model included in them as the Young 89 Model. *See e.g.* TEX 1207.0004; TEX 0104.0021; TEX 0105.0016; TEX 1467.0010; TEX 1263.0008; TEX 1285.0009; TEX 1227.0006. Further, several of these manuscripts indicate that the subject matter of the submission had been previously approved for release previously. TEX 1465.0016; TEX 1410.0002; TEX 0104.0009-11; TEX 0105.0012; TEX 1263.0003; TEX 1227.0003.

In light of the foregoing, the Court finds credible Mr. Lopez's testimony that he does not recall being aware of the specific receptor model disclosed in Young 89. Specifically, the Court finds credible Mr. Lopez's testimony that, in his review of such manuscripts, he could not recall whether he specifically saw or paid attention to the depiction of the Young 89 Model included in them. *See e.g.* T. Tr., Feb. 24, 2009 A.M. 19:20-20:12, 27:6-12 (Lopez).

The Court finds credible Mr. Lopez's testimony that he did not and would not have intentionally withhold Young 89 from the PTO because: (1) "it would be against the law and [Mr. Lopez is] an attorney and [he] wouldn't have done that" and (2) Mr. Lopez "wouldn't risk [his] license on the basis . . . [of] doing something as idiotic as attempting to deliberately hide a

document." *Id.* at 63-22-64:15. Further, the Court finds credible the testimony of Mr. Lopez that he had an understanding that he had an obligation to disclose information to the PTO that was material to the patentability of pending claims during the 1990 through 1993 time frame. *Id.* at 52:4-9. The Court also finds that, by disclosing several references to patents listing Dr. Young as an inventor, Mr. Lopez complied with his duty of candor and that, given such disclosures, there is no reason to believe that Mr. Lopez would have tried to hide a document that would be easily discoverable later. *Id.* at 62:23-63:21, 64:8-11 (Lopez); *see also* TEX 1442.0130 (disclosing several patents, including the '203 patent to Young), 0134 (disclosing two patents, including European Patent Application 0 318 and Young '093 to Young); TEX 1444.0179 (disclosing several patents, including the '203 Patent and Young '093 to Young), 0303 (disclosing several patents in an International Search Report Form, including U.S. Patent No. 4,661,499 and European Patent Application 0 206 751, both to Young), 0305 (disclosing several patents, including Young '409, Young '818 and European Patent Application 0 271 287, European Patent Application 0 233 763, and European Patent Application 0 206 751; all to Young)).

k. Singulair®

As noted above, the FDA approved the use of Singulair® tablets in 10 mg form and 5 mg form for the prophylaxis and chronic treatment of asthma in patients 15 years of age and older and pediatric patients from 6 to 14 years of age, respectively, on February 20, 1998. *Id.* at 42. The FDA subsequently approved various other dosages and forms and for the treatment of perennial and seasonal allergic rhinitis as well as for the prevention of exercise-induced bronchoconstriction ("EIB"). (Revised Final Pretrial Order, Stipulated Facts 44-47).

The Court finds compelling the testimony of Merck's expert witness, Dr. Vellturo,

regarding the commercial success of Singulair®. The Court finds that sales of Singulair® pharmaceutical products from 1998, the year it was first introduced, through 2007 totaled some $14 billion dollars. (T. Tr., Feb. 25, 2009 P.M. 88:18-25 (Vellturo)). In 2007, Singulair® sales in the United States totaled $3.0 billion dollars; worldwide totals topped $4.3 billion dollars. *Id.* at 88:23- 25. The Court also finds that as sales of Singulair® products increased, sales of Accolate®, the only other leukotriene antagonist that has been approved for sale by the FDA, have decreased. *Id.* at 91:10-19, 94:20-23, 95:1-6, 89:5-9. The Court also finds compelling the testimony of Dr. Jaffe that Merck spends less on advertising Singulair® than some of Merck's competitors do in advertising competing products and that Merck's advertising return on Singulair® products is much lower than the return received by pharmaceutical companies on average on asthma and allergic rhinitis medications. (T. Tr., Feb. 23, 2009 P.M. 118:12-15, 123:3-24, (Jaffe)).[6]

The Court also finds that, in connection with its ANDA Nos. 78-605 and 78-723, Teva submitted almost the identical labeling and package inserts as those contained in corresponding Singulair® products proposed montelukast sodium and chewable tablets. (Revised Final Pretrial Order, Stipulated Facts 6, 14; TEX 3003.0080; TEX 3009; TEX 3004.0001, 0009).

The Court further find that the other drugs available during the relevant time period showed significant shortcomings in effectively treating asthma and allergic rhinitis. The Court

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[6] The Court notes that it reserved its decision on MSD's motion in limine [Docket No. 70-2] with respect to the admissibility of Dr. Jaffe's expert testimony regarding the ghostwriting of scientific articles explaining the safety and efficacy of Singulair® as well as Dr. Jaffe's expert testimony regarding evidence pertaining to Neurotonin® and Nesiritide products. [Docket No. 101]. However, it appearing that Teva has not sought to admit such evidence into the record, the Court dismisses this motion as moot.

finds credible the testimony of Merck's expert witness Dr. Meltzer that short-acting beta agonists are only useful as "rescue" medication but not suitable for long term treatment. (T. Tr., Feb. 25, 2009 P.M. 45:8-9, 18-23, 46:5-6,11-12, 12-16 (Meltzer)). Further, the Court finds Dr. Barnes' testimony credible that inhaled corticosteroids are not particularly effective at lower doses and can cause severe side effects at higher doses. (T. Tr., Feb. 4, 2009 104:12-16, 105:8-14). The Court also finds that long acting beta agonists, which carry a "black box" warning indicating that they have side effects that are associated with increased chance of death, are never used on their own and are always used in conjunctions with inhaled corticosteroids. (T. Tr., Feb. 25, 2009 P.M. at 49:16-20, 49:21-22 (Meltzer); T. Tr., Feb. 4, 2009 81:9-22 (Barnes)).

The Court also finds credible the testimony on the efficacy of Singulair® in treating asthma and allergic rhinitis. Specifically, the Court finds that Singulair® tablets, because they are orally active and are the only LTD_4 antagonist currently on the market that is indicated for once-a-day use make the drug that is easy to take and useful in the treatment of children. (T. Tr., Feb. 25, 2009 P.M. 59:4-17, 60:6-20, 58:23-59:17, 61:6-8 (Meltzer); T. Tr., Feb. 4, 2009 66:14-16 (Barnes); Philips Dep. Tr. 184:16-20). The Court finds that these attributes also make Singulair® safer and more effective than Accolate®, the only other drug targeting the LTD_4 mediator. (T. Tr., Feb. 25, 2009 P.M. 67:18-21, 66:25-67:11, 67:11-13 (Meltzer)). The Court also finds that Singulair® is safer than zilutin, a leukotriene inhibitor that is a commercially available under the name Zyflo®, which is associated with significant liver toxicity issues. (T. Tr., Feb. 25, 2009 P.M. 67:21-68:2, 68:1-10, 13-17 (Meltzer)).

The Court also finds that the Global Initiative For Asthma ("GINA") guidelines recommend the use of montelukast as an accepted management therapy for the treatment of

asthma. (T. Tr., Feb. 4, 2009 79:17-25, 80:2-3 (Barnes)). Further, the Court finds credible the Malmstrom Paper, which compares the clinical benefits of montelukast to that of beclomethasone, an inhaled corticosteroid, and demonstrates that although that inhaled corticosteroids are more effective than montelukast for the majority of patients, that is not true for all patients. (TEX 3128 (cross-referenced as TEX 3303) at 0006). Further, the Court finds that montelukast is sometimes used as an add-on therapy to inhaled corticosteroids for patients whose asthma cannot be controlled with inhaled corticosteroids alone and that the Biernacki Paper concludes that the addition of montelukast to the therapy of patients whose asthma was otherwise uncontrolled with the use of corticosteroids alone resulted in a significant improvement in patients' quality of life. (T. Tr., Feb. 25, 2009 P.M. 65:24-66:10 (Meltzer); TEX 3292.0002; T. Tr., Feb. 4, 2009 87:3-6, 87:10-21 (Barnes)).

l. The Efforts of Others to Develop LTD_4 Antagonists

The Court also finds that other companies attempted to develop LTD_4 antagonists that are effective and safe enough for commercial use. During 1990 to 1991, SK&F developed two promising compounds and licensed another from Ono Pharmaceutical. (T. Tr., Feb. 25, 2009 A.M. 58:24-59:12, 59:19-60:7, 60:22-61:9 (Gleason)). Each of these compounds progressed to clinical trials; however they were eventually abandoned for failing to meet expectations. *Id.* at 59:9-12, 1-12, 19-60:7, 61:7-11. The Court also finds that, during this time period, several other companies, including Eli Lilly & Co., Revlon, Rhone-Poulenc Rorer, Wyeth Pharmaceuticals, Leo Pharmaceuticals, Merck, and Imperial Chemical Industries ("ICI") had compounds in advanced stages of development and that, of all of these compounds, only the ICI compound, now commercially available as Accolate®, eventually made it to commercial development. *Id.* at

61:22-63:5, 63:22-24, 64:3-4).

2. Conclusions of Law

The Court concludes that Teva has failed to prove that the '473 patent is invalid and unenforceable either because MSD acquired the '473 patent through inequitable conduct or the '473 patent was obvious under 35 U.S.C. § 103 in light of these additional prior arts.

a. Inequitable Conduct

"Patent applicants and those substantively involved in the preparation or prosecution of a patent application owe a 'duty of candor and good faith' to the PTO." *M. Eagles Tool Warehouse, Inc. v. Fisher Tooling Co.*, 439 F.3d 1335, 1339 (Fed. Cir. 2006) (quoting 37 C.F.R. § 1.56(a) (2004); *see also Molins PLC v. Textron, Inc.*, 48 F.3d 1172, 1178 (Fed. Cir. 1995)). Such a breach may constitute inequitable conduct, which can arise from a failure to disclose information material to patentability, coupled with an intent to deceive the PTO. *M. Eagles Tool Warehouse*, 439 F.3d at 1339-40 (citing *Molins*, 48 F.3d at 1178).

"The burden of proving inequitable conduct lies with the accused infringer." *Star Scientific, Inc. v. R.J. Reynolds Tobacco Co.*, 537 F.3d 1357, 1356 (Fed. Cir. 2008) (citing *Ulead Sys., Inc. v. Lex Computer & Mgmt. Corp.*, 351 F.3d 1139, 1146 (Fed. Cir. 2003)). As such, in order to prove inequitable conduct, Teva must prove by clear and convincing evidence that Merck: "(1) made an affirmative misrepresentation of material fact, failed to disclose material information, or submitted false material information, and (2) intended to deceive the [PTO]." *Cargill, Inc. v. Canbra Foods, Ltd.*, 476 F.3d 1359, 1363-64 (Fed. Cir. 2007) (citing *Impax Labs., Inc. v. Aventis Pharms. Inc.*, 468 F.3d 1366, 1374 (Fed. Cir. 2006)).

"If a district court finds that the requirements of materiality and intent have been

established by clear and convincing evidence, it must then 'balance the equities to determine whether the patentee has committed inequitable conduct that warrants holding the patent unenforceable.'" *Cargill, Inc.*, 476 F.3d at 1364 (citing *Impax Labs.*, *Inc.*, 468 F.3d at 1374 (quoting *Monsanto Co. v. Bayer Bioscience N.V.*, 363 F.3d 1235, 1239 (Fed. Cir. 2004)). However, "[i]f a threshold level of intent to deceive or materiality is not established by clear and convincing evidence, the district court does not have any discretion to exercise and cannot hold the patent unenforceable regardless of the relative equities or how it might balance them." *Star Sci.,* 537 F.3d at 1367 (citing *Nordberg, Inc. v. Telsmith, Inc*., 82 F.3d 394, 398 (Fed. Cir. 1996) (holding that the district court properly refrained from balancing materiality and intent when a threshold showing of intent to deceive was not clearly and convincingly made)). Thus, "[o]nly after adequate showings are made as to both materiality and deceptive intent may the district court look to the equities by weighing the facts underlying those showings." *Star Scientific*, 537 F.3d at 1367. Further, "even if a threshold level of both materiality and intent to deceive are proven by clear and convincing evidence, the court may still decline to render the patent unenforceable." *Star Scientific*, 537 F.3d at 1365 (citing *Monsanto*, 363 F.3d at 1239). However, in conducting such a balancing of the equities, courts generally find that "[t]he more material the omission or the misrepresentation, the lower the level of intent required to establish inequitable conduct, and vice versa." *Critikon, Inc. v. Becton Dickinson Vascular Access, Inc*., 120 F.3d 1253, 1256 (Fed. Cir. 1997).

The reason for the need for such a balancing test is that the penalty for inequitable conduct is severe. *Kingsdown Medical Consultants, Ltd. v. Hollister, Inc.*, 863 F.2d 867, 877 (Fed. Cir. 1988) ("[w]hen a court has finally determined that inequitable conduct occurred in

relation to one or more claims during prosecution of the patent application, the entire patent is rendered unenforceable.") Additionally, the Federal Circuit has expressed the concern that "the habit of charging inequitable conduct in almost every major patent case has become an absolute plague." *Burlington Industries, Inc. v. Dayco Corp*., 849 F.2d 1418, 1422 (Fed. Cir. 1988); *see also Kingsdown*, 863 F.2d at 876 ("the charge of inequitable conduct before the [PTO] had come to be attached to every patent prosecution, diverting the court from genuine issues and simply spawning satellite litigation."); *Aventis Pharma S.A. v. Amphastar Pharms., Inc*., 525 F.3d 1334, 1350 (Fed. Cir. 2008) ("At an earlier time, the Federal Circuit also observed that inequitable conduct as a litigation strategy had become a 'plague.' (citing *Burlington Indus., Inc.* 849 F.2d at 1422) (further citation omitted)). As such and in light of the severity of penalty for such a charge, "courts must be vigilant in not permitting the defense to be applied too lightly." *Star Scientific*, 537 F.3d at 1366 (reasoning that "[j]ust as it is inequitable to permit a patentee who obtained his patent through deliberate misrepresentations or omissions of material information to enforce the patent against others, it is also inequitable to strike down an entire patent where the patentee only committed minor missteps or acted with minimal culpability or in good faith.")

(1) Materiality[7]

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[7] As noted above, in its letter dated May 28, 2009 Teva argues that the PTO's decision to reexamine the '473 patent in light of the fact that several references, including Young 89, were not presented during the prosecution of the patent, is relevant to the its claim of inequitable conduct because it supports Teva's position that Young 89 is material. [Docket No. 118 at 2].

The Court finds this argument unpersuasive. The Court has found no case, nor has either party cited to one, which holds that the PTO's reexamination of a patent should be considered by a Court in its inequitable conduct analysis. As such, the Court finds the PTO's reexamination of the '473 patent irrelevant to its inquiry into Young 89's materiality.

Rule 56 of the United States Patent and Trademark Office ("PTO Rule 56") provides in relevant part:

> [I]nformation is material to patentability when it is not cumulative to information already of record or being made of record in the application, and
>
> > (1) It establishes, by itself or in combination with other information, a *prima facie* case of unpatentability of a claim, or
> >
> > (2) It refutes, or is inconsistent with, a position the applicant takes in:
> >
> > > (i) Opposing an argument of unpatentability relied on by the Office, or
> > >
> > > (ii) Asserting an argument of patentability.
>
> A *prima facie* case of unpatentability is established when the information compels a conclusion that a claim is unpatentable under the preponderance of evidence, burden-of-proof standard, giving each term in the claim its broadest reasonable construction consistent with the specification, and before any consideration is given to evidence which may be submitted in an attempt to establish a contrary conclusion of patentability.

37 C.F.R. § 1.56(b) (2006).

The prior version of this rule invoked a "reasonable examiner" standard, which stated that "information is material where there is a substantial likelihood that a reasonable examiner would consider it important in deciding whether to allow the application to issue as a patent." 37 C.F.R. § 1.56(a) (1991). However, in *Digital Control Inc. v. Charles Machine Works*, 437 F.3d 1309 (Fed. Cir. 2006), the United States Court of Appeals for the Federal Circuit ("Federal Circuit") explained that the materiality standard set forth in the current version of PTO Rule 56 did not supplant this earlier "reasonable examiner" standard. *Cargill, Inc.*, 476 F.3d at 1364 (citing 37 C.F.R. § 1.56(b)(2006), 37 C.F.R. § 1.56(a) (1991); *Digital Control*, 437 F.3d at 1316; *Impax Labs*., 468 F.3d at 1374). Instead, the Federal Circuit held that "if a misstatement or omission is

material under the new [PTO] Rule 56, it is material. Similarly, if a misstatement or omission is material under the 'reasonable examiner' standard. . . it is also material." *Cargill, Inc.*, 476 F.3d at 1364 (citing *Digital Control*, 437 F.3d at 1316).

"[M]ateriality is determined from the viewpoint of a reasonable patent examiner, and not the subjective beliefs of the patentee." *Cargill, Inc.* 476 F.3d at 1366 (quoting *Bristol-Myers Squibb Co. v. Rhone-Poulenc Rorer, Inc*., 326 F.3d 1226, 1238 (Fed. Cir. 2003) (internal citations and quotations omitted). Further, "[c]lose cases [of materiality] should be resolved by disclosure, not unilaterally by the applicant." *Cargill*, *Inc.*, 476 F.3d at 1367 (quoting *LaBounty Mfg., Inc. v. U.S. Int'l Trade Comm'n*, 958 F.2d 1066, 1076 (Fed. Cir. 1992) (internal quotations omitted). This rule stems from the policy that "applicants [should] continue to submit information for consideration by the [PTO] in applications rather than making and relying on their own determinations of materiality." *Cargill*, *Inc.*, 476 F.3d at 1367 (quoting *Critikon*, 120 F.3d at 1257 (internal quotations omitted)). However, "if the information allegedly withheld is not as pertinent as that considered by the examiner, or is merely cumulative to that considered by the examiner, such information is not material." *Molins*, 48 F.3d at 1179 (citing *Scripps Clinic & Research Found. v. Genentech, Inc*., 927 F.2d 1565, 1582, 1014-15 (Fed. Cir. 1991).

(a) Mr. Lopez's Statements Regarding the '414 Application Were Not False or Misleading

As noted above, the Court finds that Mr. Lopez's statements in the Reply to the patent examiner's rejection of the '414 application as obvious over Young '409 to be consistent with the with the testimony of several of Merck's witnesses as well as the testimony of Teva's expert, Dr. Lenz. In the Reply, Mr. Lopez states that "'[t]he present compounds differ from the art in that Q^2 is a secondary or tertiary alcohol or amine and that the present Z1/Z2 = CONR3.

Any one of these differences would render the present compounds unobvious; the combination of three substantial differences appears irrefutable.'" (TEX 1444.0609). This statement is consistent with the testimony of Dr. Jorgensen that "[t]here isn't any interchangeability . . . between primary, secondary, and tertiary alcohols. They're very different beasts." (T. Tr., Feb. 26, 2009 30:2-4, (Jorgensen)). Further, Dr. Young's testimony that a tertiary alcohol is not interchangeable with a primary alcohol also support's Mr. Lopez's assertion. (T. Tr., Feb. 23, 2009, A.M. 83:8-14, (Young)). Further, Dr. Lenz's testimony also supports Mr. Lopez's reply in that he stated that there are in fact differences between primary alcohols and secondary or tertiary alcohols, such as their chemical and metabolic properties. (T. Tr., Feb. 24, 2009 A.M. 114:12-115:6 (Lenz)).

In light of the foregoing, the Court concludes that this statement is not an affirmative misrepresentation of material fact for purposes of a determination of inequitable conduct. *Cargill,* 476 F.3d at 1363-64 (citing *Impax Labs.,* 468 F.3d at 1374).

(b) Young 89 is at Most Slightly Material

The parties stipulate that neither Young 89 nor the Young 89 Model were ever submitted to the PTO during the prosecution that resulted in the '473 patent. (Revised Final Pretrial Order, Stipulated Fact 121). Further, the record shows the Young 89 Model does not address many other factors necessary in determining the compound's structure, including: (1) the steric requirements; (2) the shape of the receptor; (3) the requisite polarity to bind with the receptor; (4) and the directionality of potential hydrogen bonds. (T. Tr., Feb. 25, 2009 A.M. 107:11-15, 107:23-108:4, (Gleason)). The record also shows that the Young 89 Model is quite broad and does not provide guidance as to how to between the many number of potential compounds that fit the model. *Id*. at 66:1-4; 72:5-9. As such, the evidence suggests that the Young 89 Model does

not indicate the use of a tertiary alcohol in the Q^2 position of a proposed LTD_4 antagonist; nor does it suggest that a tertiary alcohol would be interchangeable with a dimethyl amide. (Belley Dep. Tr. 33:3-34:3; T. Tr., Feb. 23, 2009 A.M. 118:14-119:2 (Young)).

However, the Young 89 Model does provide some general information regarding the composition of montelukast in that it identifies the three attributes that the group located at the "B" pocket of the receptor in the model must have: it must be: (1) polar; (2) not ionized; and (3) a hydrogen bond acceptor. (T. Tr. Feb. 24, 2009, A.M. 119:23-120:2; 121:16-122:4 (Lenz); PTX3283 at 3283.0002; T. Tr. Feb. 23, 2009, A.M. 98:10-99:19 (Young). Further, despite the fact that he also testified that it is unclear whether montelukast fits in the Young 89 Model, Mr. Belley testified that he first came up with the idea of using a tertiary alcohol in the Q^2 side chain after a meeting in which Dr. Young presented the Young 89 Model to him. (Belley Dep. 34:16-35:13; 68:23-69:15). In light of this fact, a reasonable examiner would consider the Young 89 Model, and therefore Young 89, to be important in deciding whether to allow MSD's application to issue as the '473 patent. 37 C.F.R. § 1.56(a) (1991); *see also Cargill, Inc.*, 476 F.3d at 1364 (citing 37 C.F.R. § 1.56(b)(2006), 37 C.F.R. § 1.56(a) (1991); *Digital Control*, 437 F.3d at 1316; *Impax Labs*., 468 F.3d at 1374).

The Court also concludes that, because the Young 89 Model is so broad and not by itself highly instructive regarding the composition of montelukast, it as well as Young 89 or only slightly material. Nevertheless, the Court also notes that "[c]lose cases [of materiality] should be resolved by disclosure, not unilaterally by the applicant." *Cargill*, *Inc.*, 476 F.3d at 1367 (quoting *LaBounty Mfg., Inc. v. U.S. Int'l Trade Comm'n*, 958 F.2d 1066, 1076 (Fed. Cir. 1992) (internal quotations omitted).

In light of the foregoing, the Court concludes that Teva has demonstrated that Young 89 and the Young 89 Model are material to the '473 patent and that MSD should have disclosed them to the PTO as prior art.

(2) Intent

As noted above, once a misrepresentation or omission is found to be material, the party challenging the validity of the patent must also demonstrate by clear and convincing evidence that the patentee intended to deceive the PTO. *Cargill, Inc.*, 476 F.3d at 1363-64 (citation omitted); *see also Ferring B.V. v. Barr Labs., Inc.*, 437 F.3d 1181, 1191 (Fed. Cir. 2006) ("Even if an omission is found to be material, the omission must also be found to have been made with the intent to deceive. 'Materiality does not presume intent, which is a separate and essential component of inequitable conduct.'" (citing *GFI, Inc. v. Franklin Corp*., 265 F.3d 1268, 1274 (Fed. Cir. 2001) (quoting *Manville Sales Corp. v. Paramount Sys., Inc*., 917 F.2d 544, 552 (Fed. Cir. 1990)). "The required showings of materiality and intent are separate, and a showing of materiality alone does not give rise to a presumption of intent to deceive." *Praxair, Inc. v. ATMI, Inc*., 543 F.3d 1306, 1313 (Fed. Cir. 2008) (citing *Kingsdown*, 863 F.2d 867 (Fed. Cir. 1988) (further citation omitted); *see also Abbott Labs. v. Sandoz, Inc*., 544 F.3d 1341, 1356 (Fed. Cir. 2008) ("Materiality is not evidence of intent, which must be established as a separate factual element of a discretionary ruling of inequitable conduct."); *Allen Organ Co. v. Kimball Int'l, Inc*., 839 F.2d 1556, 1567 (Fed Cir. 1988) ("The withholding of information must meet the thresholds of both materiality and intent . . . and absent intent to withhold it is not controlling whether the reference is found to anticipate or otherwise to be material." (citing *American Hoist & Derrick Co. v. Sowa & Sons, Inc*., 725 F.2d 1350, 1363 (Fed. Cir. 1984)).

To prove intent, a party must show that the "the involved conduct, viewed in light of all the evidence, including evidence indicative of good faith . . . indicates sufficient culpability to require a finding of intent to deceive." *Impax Labs*., 468 F.3d at 1374-75 (quoting *Kingsdown*, 863 F.2d at 876). As such,"a failure to disclose a prior art device to the PTO, where the only evidence of intent is a lack of a good faith explanation for the nondisclosure, cannot constitute clear and convincing evidence sufficient to support a determination of culpable intent." *M. Eagles Tool Warehouse*., 439 F.3d at 1341. Further, "a patentee need not offer a good faith explanation unless the accused infringer first carried his burden to prove a threshold level of intent to deceive by clear and convincing evidence." *Star Scentific.*, 537 F.3d at 1368 (citing *Nordberg* 82 F.3d at 398).

Further, "[i]ntent need not, and rarely can, be proven by direct evidence." *Impax Labs.*, 468 F.3d at 1375 (citing *Merck & Co.*, 873 F.2d at 1422). Instead, intent to deceive "is usually inferred from the facts and circumstances surrounding the conduct at issue." *Impax Labs.*, 468 F.3d at 1375 (citing *Merck & Co.*, 873 F.2d at 1422). Such an inference is appropriate when: "(1) highly material information is withheld; (2) 'the applicant knew of the information [and] . . . knew or should have known of the materiality of the information; and (3) the applicant has not provided a credible explanation for the withholding.'" *Praxair, Inc.*, 543 F.3d at 1313-14 (quoting *Ferring B.V. v. Barr Labs., Inc*., 437 F.3d 1181, 1191 (Fed. Cir. 2006); *see also Pfizer, Inc. v. Teva Pharms. USA, Inc*., 518 F.3d 1353, 1367 (Fed. Cir. 2008) (applying the standard set out in *Ferring* to conclude that no inference of intent was possible in the face of a credible good faith explanation for the withholding). Thus, although "[n]o single factor or combination of factors can be said always to require an inference of intent to mislead . . . a patentee facing a

high level of materiality and clear proof that it knew or should have known of that materiality, can expect to find it difficult to establish 'subjective good faith' sufficient to prevent the drawing of an inference of intent to mislead." *GFI, Inc.,* 265 F.3d at 1275 (citing *Critikon, Inc.*, 120 F.3d at 1257). In such circumstances, "[a] mere denial of intent to mislead (which would defeat every effort to establish inequitable conduct) will not suffice." *GFI, Inc.,* 265 F.3d at 1275 (citing *FMC Corp. v. Manitowoc Co.*, 835 F.2d 1411, 1416 (Fed. Cir. 1987)).

Deceptive intent should also be inferred where counsel "cultivate[s] ignorance, or disregard[s] numerous warnings that material information or prior art may exist, merely to avoid actual knowledge of that information or prior art." *Brasseler, U.S.A. I., L.P. v. Stryker Sales Corp*., 267 F.3d 1370, 1382 (Fed. Cir. 2001) (quoting *FMC Corp. v. Hennessy Industries, Inc*., 836 F.2d 521, 1275 n. 6 (Fed. Cir. 1987). As such, "[o]nce an attorney, or an applicant, has notice that information exists that appears material and questionable, that person cannot ignore that notice in an effort to avoid his or her duty to disclose." *Brasseler,* 267 F.3d at 1382 (citation omitted). However, "[t]here is no need for an attorney to pursue a fishing expedition to obtain information. . . . Thus, no duty to inquire arises unless counsel is on notice of the likelihood that specific, relevant, material information exists and should be disclosed." *Id.* at 1382-83. Further, a patentee cannot be found to have intentionally withheld material prior art when it is unaware of the prior art's existence. *See Nordberg*, 82 F.3d at 398 (holding that because patentee could not have "concealed" a prior art reference of which it was unaware, the district court did not clearly err in finding that the patentee did not conceal the prior art with an intent to mislead the PTO).

Conversely, a showing of conduct amounting only to gross negligence does not support an inference of an intent to deceive. *Molins*, 48 F.3d at 1181 ("While intent to deceive the PTO

may be found as a matter of inference from circumstantial evidence, circumstantial evidence cannot indicate merely gross negligence." (citing *Kingsdown*, 863 F.2d at 876) ("[A] finding that particular conduct amounts to 'gross negligence' does not of itself justify an inference of intent to deceive; the involved conduct, viewed in light of all the evidence, including evidence indicative of good faith, must indicate sufficient culpability to require a finding of intent to deceive."). To support a finding of inequitable conduct,

> "the alleged conduct must not amount merely to the improper performance of, or omission of, an act one ought to have performed. Rather, clear and convincing evidence must prove that an applicant had the specific intent to accomplish an act that the applicant ought not to have performed, viz., misleading or deceiving the PTO. In a case involving nondisclosure of information, clear and convincing evidence must show that the applicant made a deliberate decision to withhold a known material reference."

Molins, 48 F.3d at 1181. As such, "[i]ntent to deceive can not be inferred solely from the fact that information was not disclosed; there must be a factual basis for a finding of deceptive intent." *Abbott Labs*., 544 F.3d at 1355 (citing *Hebert v. Lisle Corp*., 99 F.3d 1109, 1115-16 (Fed. Cir. 1996).

(a) Teva has Failed to Put Forth Sufficient Evidence to Prove that Mr. Lopez Acted with an Intent to Deceive the PTO

The Court concludes that Teva has failed to prove by clear and convincing evidence that Mr. Lopez acted with a specific intent to deceive the PTO when he failed to submit Young 89 as prior art in the priority application that eventually matured into the '473 patent. As noted above, "[i]ntent need not, and rarely can, be proven by direct evidence," and "is usually inferred from the facts and circumstances surrounding the conduct at issue." *Impax Labs.*, 468 F.3d at 1375 (citing *Merck & Co.*, 873 F.2d at 1422). Such an inference is appropriate when: "(1) highly

material information is withheld; (2) 'the applicant knew of the information [and] . . . knew or should have known of the materiality of the information; and (3) the applicant has not provided a credible explanation for the withholding.'" *Praxair, Inc.*, 543 F.3d at 1313-14 (quoting *Ferring B.V. v. Barr Labs., Inc.*, 437 F.3d 1181, 1191 (Fed. Cir. 2006); *see also Pfizer, Inc. v. Teva Pharms. USA, Inc.*, 518 F.3d 1353, 1367 (Fed. Cir. 2008) (applying the standard set out in *Ferring* to conclude that no inference of intent was possible in the face of a credible good faith explanation for the withholding).

However, an inference of deceptive intent is not warranted in this case because, as noted above, the Court concludes that Young 89 is only slightly, and not highly, material. The Court notes that Teva has put forth evidence that Mr. Lopez had approved for release a manuscript of what was eventually published as Young 89 as well as several other manuscripts that included copies of the Young 89 Model. (TEX 1410; Stipulated Fact 26; T. Tr., Feb. 24, 2009 A.M. 12:18-41:25; DTX 1207, DTX 1411, DTX 1285, DTX 104, DTX 105, DTX 1467, DTX 1263, DTX 1465, DTX 1227). However, the Court also notes that Mr. Lopez testified that he could not recall whether he specifically saw or paid attention to the depiction of the Young 89 Model included in them. (T. Tr., Feb. 24, 2009 A.M. 19:20-20:12, 27:6-12 (Lopez)). Mr. Lopez also testified that he reviewed 100 or so manuscript approvals on an annual basis and that such reviews made up only a small portion of his job responsibilities and that, because of this large workload, he read less of a proposed manuscript if there were indications that suggested to him that approval of the manuscript would not be problematic and that factors that would influence Mr. Lopez's decision regarding how much time he would spend reviewing a manuscript include whether: (1) the author, especially an author that Mr. Lopez trusted, indicated that there was

nothing in the manuscript that had not been approved before; (2) a patent had been issued regarding the subject matter of the manuscript; or (3) a patent application had been filed regarding the subject matter of the manuscript. (T. Tr., Feb. 24, 2009 A.M. 60:7-15, 60:16-61:3, 61:13-25, (Lopez)). Teva argues that this assertion is rebutted by the fact that the manuscript for Young 89 includes Mr. Lopez's handwritten note which contradicts the statement on the manuscript that multiple patent applications had already been filed covering the it's subject matter, and asserts that this note indicates that Mr. Lopez reviewed this manuscript in its entirety. (TEX 1410; T. Tr., Feb. 24, 2009 A.M. 70:11-22; TEX 1410 at MSD02113350). However, this evidence alone is insufficient to meet Teva's high burden of having to prove by clear and convincing evidence that Mr. Lopez acted with an intent to deceive the PTO.

In light of the foregoing, Teva has at most put forth circumstantial evidence that might support a conclusion that Mr. Lopez's failure to disclose Young 89 to the PTO arguably amounts to negligence. However, even "a finding that particular conduct amounts to 'gross negligence' does not of itself justify an inference of intent to deceive." *Kingsdown*, 863 F.2d at 876 (reasoning that "the involved conduct, viewed in light of all the evidence, including evidence indicative of good faith, must indicate sufficient culpability to require a finding of intent to deceive."; *see also Molins*, 48 F.3d at 1181 ("While intent to deceive the PTO may be found as a matter of inference from circumstantial evidence, circumstantial evidence cannot indicate merely gross negligence.)

(3) A Balancing of the Equities is Not Warranted

As noted above, "[i]f a district court finds that the requirements of materiality and intent have been established by clear and convincing evidence, it must then 'balance the equities to

determine whether the patentee has committed inequitable conduct that warrants holding the patent unenforceable.'" *Cargill, Inc.*, 476 F.3d at 1364 (internal citations omitted). However, "[i]f a threshold level of intent to deceive or materiality is not established by clear and convincing evidence, the district court does not have any discretion to exercise and cannot hold the patent unenforceable regardless of the relative equities or how it might balance them." *Star Sci.,* 537 F.3d at 1367 (internal citation omitted).

In the instant case, the Court concludes that Teva has failed to show that Mr. Lopez withheld Young 89 from the PTO with an intent to deceive. As such, a balancing of the equities to determine whether MSD has committed inequitable conduct is not warranted. *Cargill, Inc.*, 476 F.3d at 1364

b. Obviousness

"Under 35 U.S.C. § 282 a patent is presumed valid, and proof of its invalidity requires 'clear and convincing' evidence." *Intel. Corp. v. U.S. Int'l Trade Comm'n*, 946 F.2d 821, 830 (Fed. Cir. 1991) (quoting *Buildex, Inc. v. Kason Indus., Inc*., 849 F.2d 1461 (Fed. Cir. 1988)); *see also Takeda Chem. Indus. v. Alphapharm Pty., Ltd..,* 492 F.3d 1350, 1355 (Fed. Cir. 2007). However, a patent may be invalidated if a claim in the patent is shown to be obvious as defined by 35 U.S.C. § 103(a), which provides in relevant part:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

35 U.S.C. § 103(a).

Obviousness depends on: (1) "the scope and content of the prior art"; (2) the "differences between the prior art and the claims"; (3) "the level of ordinary skill in the pertinent art"; and (4) "[s]uch secondary considerations as commercial success, long felt but unsolved needs, failure of others, etc." *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 406 (2007), (citing *Graham v. John Deere Co.*, 383 U.S. 1, 17 (1966)).

Given the presumption of validity surrounding a patent granted by the PTO, invalidity of the patent through obviousness must be proven by clear and convincing evidence. *PIN/NIP, Inc. v. Platte Chem. Co.*, 304 F.3d 1235, 1243 (Fed. Cir. 2002).[8] Further, failure to show *prima facie* obviousness means the claims are not deemed invalid for obviousness, thereby ending the inquiry. *Yamanouchi Pharm. Co. v. Danbury Pharmacal, Inc.*, 231 F.3d 1339, 1345 (Fed. Cir. 2000) (holding that because defendants failed to show even a *prima facie* case for obviousness, the court need not separately address, the objective evidence of non-obviousness); *see also Kaufman Co. v. Lantech, Inc.,* 807 F.2d 970, 974-75 (Fed. Cir. 1986) (holding that plaintiff failed to meet its burden of showing obviousness in view of prior art by clear and convincing evidence, and so the Court need not consider patentee's additional rebuttal evidence of non-obviousness).

However, "[o]nce a challenger has presented a *prima facie* case of invalidity, the patentee has the burden of going forward with rebuttal evidence." *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d

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[8]The Court notes that, in *KSR*, the Supreme Court commented that the rationale for the presumption of a patent's validity, namely, that the PTO has previously approved the claim, is "much diminished" when prior art that is relevant obviousness inquiry is not before the examiner during the prosecution of the patent. *KSR*, 550 U.S. at 426. However, the Supreme Court did not hold that, under such circumstances, the standard for proving invalidity should be reduced to the preponderance of the evidence standard, as Teva contends. (Teva's Concl. of Law on Obviousness, at ¶ 2 [Docket No. 113]).

1348, 1360 (Fed. Cir. 2007) (citing *Mas-Hamilton Group v. LaGard, Inc*., 156 F.3d 1206, 1216 (Fed. Cir. 1998) (citing *Hybritech Inc. v. Monoclonal Antibodies, Inc*., 802 F.2d 1367, 1376 (Fed. Cir. 1986)); *see also Cable Elec. Prods. Inc. v. Genmark, Inc.*, 770 F.2d 1015, 1022 (Fed. Cir. 1985), ("[I]f evidence is presented establishing a *prima facie* case of invalidity, the opponent of invalidity must come forward with evidence to counter the *prima facie* challenge to the presumption of section 282") *overruled on other grounds by Midwest Indus., Inc. v. Karavan Trailers, Inc*., 175 F.3d 1356 (Fed. Cir. 1999). "However, this requirement does not 'in substance shift the burden of persuasion' . . . because 'the presumption of validity remains intact and the ultimate burden of proving invalidity remains with the challenger throughout the litigation.'" *Pfizer*, 480 F.3d at 1360 (quoting *Cable Elec*., 770 F.2d at 1022; *Mas-Hamilton Group*, 156 F.3d at 1216 (citing *Innovative Scuba Concepts, Inc. v. Feder Indus., Inc*., 26 F.3d 1112, 1115 (Fed. Cir. 1994)); *see also Ashland Oil, Inc. v. Delta Resins & Refractories, Inc.*, 776 F.2d 281, 287 (Fed. Cir. 1985)).

(1) The Test for Determining Obviousness, *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398 (2007)

The Federal Circuit previously applied a test to determine obviousness, known as the "teaching, suggestion or motivation" test (the "TSM test"). *KSR*, 550 U.S. at 407-08. Under this test, a "patent claim is only proved obvious if 'some motivation or suggestion to combine the prior art teachings' can be found in the prior art, the nature of the problem, or the knowledge of a person having ordinary skill in the art." *Id.* at 407 (internal citation omitted). The continuing validity of the TSM test was called into question in *KSR*. *Id.* at 415-16. While the Supreme Court did not reject the TSM test outright, it did reject the Federal Court of Appeals' rigid application of the test. *Id.*

However, in *KSR Int'l Co. v. Teleflex Inc.*, the Supreme Court instructed courts to evaluate the four Graham factors using a "broad inquiry" and employing a "common sense" approach. *See id.* at 418-20. The Court explained that "common sense" dictates that "familiar items may have obvious uses beyond their primary purposes, and in many cases a person of ordinary skill will be able to fit the teachings of multiple patents together like pieces of a puzzle." *Id*. at 420. However, the Supreme Court also held that "[a]lthough common sense directs one to look with care at a patent application that claims as innovation the combination of two known devices according to their established functions, it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does." *Id.* at 418. The Supreme Court held that "[t]his is so because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known." *Id.* at 419. As such, in determining obviousness, a court must inquire into whether there is "any need or problem known in the field of endeavor at the time of invention and addressed by the patent can provide a reason for combining the elements in the manner claimed." *Id.* at 420. The Court also cautioned against "distortion caused by hindsight bias and . . . arguments reliant upon ex post reasoning." *Id.* at 421(citing *Graham*, 383 U.S. at 36 (warning against a "temptation to read into the prior art the teachings of the invention in issue"and instructing courts to "'guard against slipping into use of hindsight'" (further citation omitted)).

(2) Person of Ordinary Skill in the Art

Section 103 provides that obviousness must be determined from the perspective of "a person having ordinary skill in the art to which said subject matter pertains." 35 U.S.C. § 103(a).

Courts "thus consider whether a person of ordinary skill in the art would have been motivated to combine the prior art to achieve the claimed invention and whether there would have been a reasonable expectation of success in doing so." *Dystar Textilfarben GmbH v. C.H. Patrick Co.*, 464 F.3d 1356, 1360 (Fed. Cir. 2006). In making such a determination, "[o]ften, it will be necessary for a court to look to . . . and the background knowledge possessed by a person having ordinary skill in the art . . . in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue. *KSR*, 550 U.S. at 418. "The person of ordinary skill in the art is a hypothetical person who is presumed to know the relevant prior art." *In re GPAC Inc.*, 57 F.3d 1573, 1579 (Fed. Cir. 1995) (citing *Custom Accessories, Inc. v. Jeffrey-Allan Indus., Inc.*, 807 F.2d 955, 962 (Fed. Cir. 1986)).

In determining this skill level, courts may consider various factors including: (1) the "type of problems encountered in the art;" (2) "prior art solutions to those problems;" (3) the "rapidity with which innovations are made;" (4) the "sophistication of the technology;" and (5) the "educational level of active workers in the field." *GPAC*, 57 F.3d at 1579 (citing *Custom Accessories*, 807 F.2d at 962). However, not every factor must be present and one or more factors may predominate. *GPAC*, 57 F.3d at 1579 (citing *Custom Accessories*, 807 F.2d at 962).

"Because patentability is assessed from the perspective of the hypothetical person of ordinary skill in the art, information regarding the subjective motivations of inventors is not material." *Life Techs., Inc. v. Clontech Lab., Inc.*, 224 F.3d 1320, 1325 (Fed. Cir. 2000) (citing *Standard Oil Co. v. Am. Cyanamid Co.*, 774 F.2d 448, 454 (Fed. Cir. 1985) (noting that the person of ordinary skill in the art is an objective legal construct presumed to think along conventional lines without undertaking to innovate, whether by systematic research or by

extraordinary insights)).

(a) The Level of Skill in the Art in the Instant Case

The parties disagree as to is what the appropriate definition of a person of ordinary skill in the art in the instant case. In essence, the parties disagree regarding whether a person of ordinary skill in the art should be required to have substantial work experience in the field of leukotriene antagonists. MSD argues that one of ordinary skill in the art should have *"*substantial training in the chemical and biological sciences with an advanced degree in chemistry, training in the areas of synthetic organic chemistry and medicinal chemistry, *and substantial experience working in the research and development of leukotriene antagonists*." (Revised Final Pretrial Order at 24, ¶ 99) (emphasis added). In contrast, Teva now contends that actual experience working with leukotriene antagonists is not necessary and instead, a person of ordinary skill in the art simply "would have understood the prior art references and have the capacity to draw inferences from them, individually and overall, in designing LTD_4 antagonists." As MSD notes, Teva included a different definition, one which required "experience working in research and development of leukotriene antagonists and leukotriene biosynthesis inhibitors" in its paragraph IV certification notice. (TEX 3005.0006-0007).

The Court concludes, as a matter of law, the definition of the level of skill in the art in the instant case is one with substantial training in the chemical and biological sciences with an advanced degree in chemistry, training in the areas of synthetic organic chemistry and medicinal chemistry, and who has substantial experience working in the research and development of leukotriene antagonists *or* who understands the prior art references and have the capacity to draw inferences from them, individually and overall, in designing LTD_4 antagonists. As such,

both Dr. Gleason, MSD's expert, and Dr. Lenz, Teva's expert meet this definition. The Court concludes that both witnesses have the requisite educational backgrounds. (T. Tr., Feb. 25, 2009 A.M. 41:10-13 (Gleason); T. Tr., Feb. 24, 2009 A.M. 74:21-75:7 (Lenz)). Further, Dr. Gleason was a leader of SK&F's leukotriene antagonist program from late-1979/early-1980 through the early 1990s. (T. Tr., Feb. 25, 2009 A.M. 42:17-21, 43:3-15 (Gleason)). Additionally, although Dr. Lenz he testified that he read approximately 50 articles on leukotriene antagonists before rendering his opinion, although some of these articles were published after the 1990 to 1991 time frame. T. Tr., Feb. 24, 2009 A.M. 136:3-5, 138:10-15, 138:16-139:3 (Lenz).

(3) Comparing the Patent Claims and Prior Art

When comparing the patent claims with prior art, the "structural similarity between claimed and prior art subject matter, proved by combining references or otherwise, where the prior art gives reason or motivation to make the claimed compositions, creates a *prima facie* case of obviousness." *Takeda*, 492 F.3d at 1356 (quoting *In re Dillon*, 919 F.2d 688, 692 (Fed. Cir. 1990) (internal quotations omitted)). Further, "a *prima facie* case of obviousness also requires a showing of 'adequate support in the prior art' for the change in structure." *Takeda*, 492 F.3d at 1356 (quoting *In re Grabiak*, 769 F.2d 729, 731-32 (Fed. Cir. 1985)); *see also Eisai Co. Ltd. v. Dr. Reddy's Labs., Ltd*, 533 F.3d 1353, 1356-57 (Fed. Cir. 2008) holding that, when assessing the obviousness of a chemical compound, "the analysis of the third Graham factor (the differences between the claimed invention and the prior art) often turns on the structural similarities and differences between the claimed compound and the prior art compounds." (citing *Eli Lilly & Co. v. Zenith Goldline Pharms*., *Inc.*, 471 F.3d 1369, 1377 (Fed. Cir. 2006) (noting that, for a chemical compound, a *prima facie* case of obviousness requires "structural similarity between

claimed and prior art subject matter . . . where the prior art gives reason or motivation to make the claimed compositions" (internal citation omitted)).

The reason for this is because "close or established '[s]tructural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds.'" *Takeda* 492 F.3d at 1356 (internal citation omitted). Further, "[a] known compound may suggest its homolog, analog, or isomer because such compounds 'often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties.'" *Takeda* 492 F.3d at 1356 (quoting *Deuel*, 51 F.3d at 1558). However, "in order to find a *prima facie* case of unpatentability in such instances, a showing that the 'prior art would have suggested making the specific molecular modifications necessary to achieve the claimed invention' [is] also required." *Takeda* 492 F.3d at 1356 (quoting *Deuel*, 51 F.3d at 1558.)

Additionally, "[w]here the creation of a chemical compound requires the chemist to pursue several steps in manipulating a compound revealed in the prior art, the patent challenger must show that one of ordinary skill in the art would have had sufficient motivation to take each of those steps." *Takeda Chem. Indus. v. Mylan Labs., Inc.*, 417 F. Supp. 2d 341, 371 (S.D.N.Y. 2006) (citing *Yamanouchi,* 231 F.3d at 1344-45). Nevertheless, "obviousness cannot be avoided simply by a showing of some degree of unpredictability in the art" as long as there is a reasonable expectation of success. *Pfizer*, 480 F.3d at 1364 (citing *In re Corkill*, 771 F.2d 1496, 1500 (Fed. Cir. 1985) ("Although [the inventor] declared that it cannot be predicted how any candidate will work in a detergent composition, but that it must be tested, this does not overcome [the prior art's] teaching that hydrated zeolites will work.") (further citations omitted)

(4) Lead Compound

"Obviousness based on structural similarity . . . can be proved by identification of some motivation that would have led one of ordinary skill in the art to select and then modify a known compound (i.e. a lead compound) in a particular way to achieve the claimed compound." *Eisai*, 533 F.3d at 1357 (citation omitted). This is the case even after the Supreme Court's decision in *KSR*. *See id*. at 1360 ("post-*KSR*, a *prima facie* case of obviousness for a chemical compound still, in general, begins with the reasoned identification of a lead compound.")

KSR assumes that there is a starting reference point in the art prior to the time of invention that may lead one of skill in the art to identify a problem and pursue a potential solution. *Id* at 1359. *KSR* also presumes that the record prior to the time of invention would give a person skilled in the art some reason to make particular modifications to achieve the claimed compound. *Id.* (citing *Takeda*, 492 F.3d at 1357 ("Thus, in cases involving new chemical compounds, it remains necessary to identify some reason that would have led a chemist to modify a known compound in a particular manner to establish *prima facie* obviousness of a new claimed compound."). Further, *KSR* assumes that the record before the time of invention gives some reasons for narrowing the prior art universe to a "finite number of identified, predictable solutions," *Id.* (citing *KSR*, 550 U.S. at 421; *Ortho-McNeil Pharm., Inc. v. Mylan Labs., Inc*., 520 F.3d 1358, 1364 (Fed. Cir. 2008) (this "easily traversed, small and finite number of alternatives . . . might support an inference of obviousness.")). Thus, "[t]o the extent an art is unpredictable, as the chemical arts often are, *KSR*'s focus on these 'identified, predictable solutions' may present a difficult hurdle because potential solutions are less likely to be genuinely predictable." *Eisai*, 533 F.3d at 1359.

One cannot use the benefit of hindsight in choosing a lead compound. *Ortho-McNeil*, 520 F.3d at 1364 (*"*In other words, [alleged infringer's expert] simply retraced the path of the inventor with hindsight, discounted the number and complexity of the alternatives, and concluded that the invention . . . was obvious. Of course, this reasoning is always inappropriate for an obviousness test based on the language of Title 35 that requires the analysis to examine 'the subject matter as a whole' to ascertain if it 'would have been obvious at the time the invention was made.'" (quoting 35 U.S.C. § 103(a)).

(5) Teva Has Failed to Put Forth Sufficient Evidence that the '473 Patent is Obvious in Light of the Prior Art.

The Court concludes that Teva has not proven by clear and convincing evidence that the '473 patent is obvious in light of the prior art. Specifically, Teva's choice of a lead structure and its obviousness analysis on which it is based does not demonstrate that the prior art would lead a person skilled in the art to discover montelukast.

In choosing a lead structure, Dr. Lenz did not choose an actual compound but instead chose a concept for a compound. T. Tr., Feb. 24, 2009 P.M. 14:19-22 (Lenz). Dr. Lenz made this choice despite the fact that, as of April 1991, at least ten compounds in the area of leukotriene antagonists existed that were in preclinical or clinical evaluations and for which biological assay data available. (T. Tr., Feb. 24, 2009 P.M. 13:24-14:11, 33:17-34:3, 14:12-14, 14:17-18, 34:1- (Lenz)). Further, the record shows that Teva's analysis requires at least eleven distinct steps from L-660,711 to Teva's lead structure to compound 97 to montelukast, all without the benefit of biological assay data. (T. Tr., Feb. 25, 2009 A.M. 9:2-5, 9-14, 15-10:7, 10:8-10, 12:21-13:7, 13:12-1, 15:7-10, 15:11-21, 16:18-25, 17:1-7, 17:8-10, 17:11-14, 17:15-18:21, 18:9-14 (Lenz)).

Dr. Lenz has not supplied a basis or motivation sufficient to have led one of ordinary skill in the art to select and then modify this hypothetical lead structure in order to achieve the claimed compound. *Eisai*, 533 F.3d at 1357 (citation omitted). For example, Dr. Lenz does not provide convincing evidence to explain why the Q^2 side chain should contain a phenyl ring and his assertion that such a modification is necessary and logical is contradicted by Dr. Gleason. (T. Tr. Feb.24, 2009 P.M.44:22-45:2, (Lenz); (T. Tr. Feb. 25, 2009 A.M. at 91:21-92:2, (Gleason)). Additionally, the record shows that the Young 89 Model does not teach not teach that a primary alcohol would be interchangeable with either a secondary or a tertiary alcohol; thus Dr. Lenz's choice to do so is also without sufficient motivation. (T. Tr., Feb. 23, 2009 A.M. 79:15-80:2, 83:8-14 (Young); T. Tr., Feb. 26, 2009 29:2-4, 29:20-23, 30:2-4 (Jorgensen); Tr., Feb. 25, 2009 A.M. 49:25-50:50, (Gleason); Belley Dep. Tr. 33:3-34:3).

Further with respect to the lengthening of the Q^1 side chain, the Perchonock Paper, which was the only literature available at the time that provided some guidance on this issue, actually taught that lengthening the Q^1 side chain led to undesirable effects. (T. Tr. Feb. 24. 2009 P.M. 70:15-22, 71:13-15, (Lenz)). Further, despite Dr. Lenz's assertions to the contrary, two publications, the Newton Paper and the Hay Paper, indicate that beta-oxidation of the Q^1 side chain would not have been a concern of a person skilled in the art. (TEX 3360; TEX 3141; T. Tr., Feb. 24, 2009 P.M. 73:16-24, 76:1-7, 76:25- 77:2, (Lenz)). Additionally, even if beta-oxidation were a concern, the record also teaches against Dr. Lenz's solution of substituting cyclopropyl groups for the two methyl groups, because cyclopropyl groups were not easy to make and not that commonly used. (T. Tr., Feb. 25, 2009 A.M. 100:10-19., (Gleason)). In light of the foregoing, Teva's lead compound and the obviousness analysis upon which it is based does not

set forth a *prima facie* case of obviousness.

The Court also concludes that Teva impermissibly used hindsight in order to choose a lead compound. As noted above, it is impermissible to use the benefit of hindsight in choosing a lead compound. *Ortho-McNeil*, 520 F.3d at 1364 (internal citation omitted). Here, the record shows that Dr. Lenz applied four filters to come up with his lead compound structure and to find that compound 97 would have been particularly preferred because of the dimethyl amide at the "X" position of his generic lead structure. (T. Tr., Feb. 24, 2009 P.M. 46:3-5, 49:5-7 (Lenz)). However, the record also shows that several other compounds, compounds 402, 409, 410, and 420 of the '882 patent also satisfy his four filters, even when the preferred and more restrictive criteria that "X" be a dimethyl amide is applied. *Id.* at 48:11-13, 49:16-18, 49:22-50:3, 50:14-16. The Court concludes that in abandoning these other compounds and focusing on compound 97, Dr. Lenz impermissibly used the benefit of hindsight to eliminate compounds with structures that he perceived would require more modifications to get to montelukast.

(5) Secondary Considerations

When determining whether a claim is obvious, courts must also consider secondary considerations such as commercial success, long-felt but unsolved needs, failure of others, and unexpected results. *KSR.*, 550 U.S. at 406, (citing *Graham*, 383 U.S. at 17); *see Ruiz v. A.B. Chance Co.*, 234 F.3d 654, 662-63 (Fed. Cir. 2000). Such objective secondary considerations can "often be the most probative and cogent evidence in the record" in that they "may often establish that an invention appearing to have been obvious in light of the prior art was not." *Stratoflex, Inc. v. Aeroquip Corp.*, 713 F.2d 1530, 1538 (Fed. Cir. 1983). As such, objective evidence of such considerations "must be considered before a conclusion on obviousness is reached and is not

merely 'icing on the cake.'" *Hybritech*, 802 F.2d at 1380.

However, secondary considerations, "do not necessarily control the obviousness conclusion." *Pfizer*, 480 F.3d at 1372 (citing *Newell Cos., Inc. v. Kenney Mfg. Co.*, 864 F.2d 757, 768 (Fed. Cir. 1988)). In order to be given substantial weight in an obviousness decision, "a nexus between the merits of the claimed invention and evidence of secondary considerations is required." *Ruiz v. A.B. Chance Co.*, 234 F.3d 654, 668 (Fed. Cir. 2000).

(a) Commercial Success

"Commercial success is relevant because the law presumes an idea would successfully have been brought to market sooner, in response to market forces, had the idea been obvious to persons skilled in the art." *Merck & Co. v. Teva Pharms. USA, Inc.*, 395 F.3d 1364, 1376 (Fed. Cir. 2005). "Thus, the law deems evidence of (1) commercial success, and (2) some causal relation or 'nexus' between an invention and commercial success of a product embodying that invention, probative of whether an invention was non-obvious." *Id.*; *see also Brown & Williamson Tobacco Corp. v. Philip Morris, Inc.*, 229 F.3d 1120, 1130 (Fed. Cir. 2000) (citing *J.T. Eaton & Co. v. Atl. Paste & Glue Co.*, 106 F.3d 1563, 1571,(Fed. Cir. 1997); *Demaco Corp. v. F. Von Langsdorff Licensing Ltd.*, 851 F.2d 1387, 1392 (Fed. Cir. 1988)).

However, "[i]t is not necessary . . . that the patented invention be solely responsible for the commercial success, in order for this factor to be given weight appropriate to the evidence, along with other pertinent factors." *Continental Can Co., Inc. v. Monsanto Co., Inc.*, 948 F.2d 1264, 1273 (Fed. Cir. 1991) (citing *Demaco*, 851 F.2d at 1392-94; *Rosemount, Inc. v. Beckman Instruments, Inc.*, 727 F.2d 1540, 1546 (Fed. Cir. 1984). Further, "[a] patentee is *not* required to prove as part of its *prima facie* case that the commercial success of the patented invention is not

due to factors other than the patented invention." *Demarco*, 851 F.2d at 1394 (emphasis in original). Instead, a patentee need only demonstrate that the commercial success was of the patented invention itself. *Id.* (holding that "[a] requirement for proof of the negative of all imaginable contributing factors would be unfairly burdensome, and contrary to the ordinary rules of evidence.")

Further, if the marketed product embodies the claimed features and is coextensive with them, a nexus is presumed and the burden shifts to the party asserting obviousness to present evidence to rebut that presumption. *Brown*, 229 F.3d at 1130 (citing *J.T. Eaton*, 106 F.3d at 1571; *Demaco*, 851 F.2d at 1392-93). This presumption cannot be rebutted with mere argument; rather evidence must be put forth. *Brown*, 229 F.3d at 1130 (citing *Demaco*, 851 F.2d at 1393).

The Court concludes that there is sufficient evidence that Singulair® is a commercial success and a 'nexus' exists between the '473 patent and Singulair®'s commercial success. The record shows that sales of Singulair® pharmaceutical products from 1998, the year it was first introduced, through 2007 totaled some $14 billion dollars. (T. Tr., Feb. 25, 2009 P.M. 88:18-25 (Vellturo)). Further, as sales of Singulair® products increased, sales of Accolate®, the only other leukotriene antagonist that has been approved for sale by the FDA, have decreased. *Id.* at 91:10-19, 94:20-23, 95:1-6, 89:5-9. Although Teva contends that Singulair®'s success is due to its extensive promotional activities aimed at both consumers and doctors, this argument is belied by the testimony of Teva's expert, Dr. Jaffe, that Merck spends less on advertising Singulair® than some of Merck's competitors do on competing products and that Merck's advertising return on Singulair® products is much lower than the return received by pharmaceutical companies on average on asthma and allergic rhinitis medications. (T. Tr., Feb. 23, 2009 P.M. 118:12-15,

123:3-24, (Jaffe)).

Further, as noted above, it is not required that MSD prove that Singulair®'s commercial success is not due to factors other than the patented invention. *Demarco*, 851 F.2d at 1394 (emphasis in original). Instead, MSD need only demonstrate that the commercial success was of the patented invention itself. *Id.* The Court concludes that MSD met this burden.

(b) Long-Felt But Unsolved Need

Evidence of a long-felt but unsolved need for the invention is also an indicator of non-obviousness. *Graham*, 383 U.S. at 17-18. Long-felt need is not analyzed only as of the date of the most pertinent prior art references. Rather, it is "analyzed as of the date of an articulated identified problem and evidence of efforts to solve that problem." *Texas Instruments v. U.S. Int'l Trade Comm'n*, 988 F.2d 1165, 1178 (Fed. Cir. 1993).

The Court concludes that Singulair® met a long-felt but unsolved need in the treatment of asthma and allergic rhinitis. The record shows that other drugs available prior to montelukast's inception showed significant shortcomings. For example, the record indicates that short-acting beta agonists are only useful as "rescue" medication but not suitable for long term treatment. (T. Tr., Feb. 25, 2009 P.M. 45:8-9, 18-23, 46:5-6,11-12, 12-16 (Meltzer)). The record also shows that inhaled corticosteroids are not particularly effective at lower doses and can cause severe side effects at higher doses. (T. Tr., Feb. 4, 2009 104:12-16, 105:8-14). Further, long acting beta agonists, which carry a "black box" warning indicating that they have side effects that are associated with increased chance of death, are never used on their own and are always used in conjunctions with inhaled corticosteroids. (T. Tr., Feb. 25, 2009 P.M. at 49:16- 20, 49:21-22 (Meltzer); T. Tr., Feb. 4, 2009 81:9-22 (Barnes)).

The conclusion that Singulair® met a long-felt need is further bolstered by the evidence of montelukast's efficacy. The record shows that because Singulair® tablets are orally active and are the only LTD_4 antagonist currently on the market that is indicated for once-a-day use, the drug that is easy to take and useful in the treatment of children. (T. Tr., Feb. 25, 2009 P.M. 59:4-17, 60:6-20, 58:23-59:17, 61:6-8 (Meltzer); T. Tr., Feb. 4, 2009 66:14- 16 (Barnes); Philips Dep. Tr. 184:16-20). These attributes also make Singulair® safer and more effective than Accolate® and the leukotriene inhibitor Zyflo®, which isassociated with significant liver toxicity issues. (T. Tr., Feb. 25, 2009 P.M. 67:18-21, 66:25-67:11, 67:11-13, 67:21-68:2, 68:1-10, 13-17 (Meltzer)).

Although Teva argues that montelukast does not fulfill a long-felt but unsolved need because studies show that inhaled corticosteroids are more effective than montelukast for the majority of patients, that is not true for all patients, the Malmstrom Paper demonstrates that this is not true for all patients. (TEX 3128 (cross-referenced as TEX 3303) at 0006). Further, the GINA guidelines recommend the use of montelukast as an accepted management therapy for the treatment of asthma. (T. Tr., Feb. 4, 2009 79:17-25, 80:2-3 (Barnes)). In light of the foregoing, it is clear that montelukast fulfills a long-felt but unsolved need for asthma and allergic rhinitis sufferers.

(c) Unexpected Results

"A *prima facie* case of obviousness based on structural similarity is rebuttable by proof that the claimed compounds possess unexpectedly advantageous or superior properties." *Application of Payne*, 606 F.2d 303, 316 (C.C.P.A. 1979) (citing *In re Papesch*, 315 F.2d 381, 386-87 (C.C.P.A. 1963)). In order to demonstrate "unexpected results," a patentee must show that the "the claimed invention exhibits some superior property or advantage that a person of

ordinary skill in the relevant art would have found surprising or unexpected." *Ortho-McNeil Pharm., Inc. v. Mylan Labs., Inc.,* 348 F. Supp. 2d 713,749 (N.D.W.V. 2004) (quoting *In re Soni*, 54 F.3d 746, 750 (Fed. Cir. 1995) (internal quotations omitted)). "Evidence that a compound is unexpectedly superior in one of a spectrum of common properties . . . can be enough to rebut a *prima facie* case of obviousness." *Ortho-McNeil*, 348 F. Supp 2d at 755 (quoting *In re Chupp*, 816 F.2d 643, 647 (Fed. Cir. 1987) (quotation omitted)). Further, in order to establish unexpected results, a patentee must show that the results were unexpected in light of the state of scientific knowledge at the time of the invention, i.e. the prior art. *See In re Geisler*, 116 F.3d 1465, 1469 (Fed. Cir. 1997).

The Court also concludes that montelukast exhibits superior properties that a person of ordinary skill in the relevant art would have found surprising or unexpected and *Ortho-McNeil,* 348 F. Supp. 2d at 749 (quoting *In re Soni*, 54 F.3d 746, 750 (Fed. Cir. 1995) (internal quotations omitted). The record shows that several of Merck's scientists were surprised at the effectiveness of the use of a tertiary alcohol for the Q^2 side chain. *See* T. Tr., 2/23/2009 A.M. 79:15-80:2, (Young); T. Tr., 2/26/2009 29:20-23, (Jorgensen) "[t]ertiary alcohols, particularly benzylic or allylic, are unstable and are expected to decompose in even mildly acidic conditions. So it is very unusual to see a tertiary alcohol on a drug." Belley Dep. Tr. 37:7-15, 54:18-24, testifying that, after he synthesized a compound containing a tertiary alcohol, "everybody was surprised to see its activity. They were surprised because it was active. They were surprised because it was more active than everything else at the time, and later there were surprised because it had good pharmacokinetics." ; Zamboni Dep. Tr. 35:17-21.) As such, this secondary consideration also weighs against the obviousness of the '473 patent.

(d) Failure of Others

Courts also consider the failed attempts of others as an objective indicia of obviousness of a claimed compound. *See Advanced Display Sys. v. Kent State Univ*., 212 F.3d 1272, 1285 (Fed. Cir. 2000) (reasoning that "evidence of failed attempts by others could be determinative on the issue of obviousness.). Further, evidence of failure by others can be demonstrated in several ways, including the use of expert testimony, scientific papers and patents." *Electro Sci. Indus. v. Gen. Scanning, Inc*., 247 F.3d 1341, 1351 (Fed. Cir. 2001).

The Court concludes that MSD has also put forth sufficient evidence of the failed attempts of others to develop a leukotriene antagonist to demonstrate that montelukast is not obvious. Several companies unsuccessfully attempted to develop LTD_4 antagonists that are effective and safe enough for commercial use. During 1990 to 1991, SK&F developed two promising compounds and licensed another from Ono Pharmaceutical. (T. Tr., Feb. 25, 2009 A.M. 58:24-59:12, 59:19-60:7, 60:22-61:9 (Gleason)). Each of these compounds progressed to clinical trials but were eventually abandoned for failing to meet expectations. *Id.* at 59:9-12, 1-12, 19-60:7, 61:7-11. Further Eli Lilly & Co., Revlon, Rhone-Poulenc Rorer, Wyeth Pharmaceuticals, Leo Pharmaceuticals, Merck, and Imperial Chemical Industries ("ICI") each had compounds in advanced stages of development; however; only the ICI compound now commercially available as Accolate®, made it to commercial development. *Id.* at 61:22-63:5, 63:22-24, 64:3-4). In light of the foregoing, the evidence of the failure of others to develop a commercially useful leukotriene antagonist weighs against a conclusion that the '473 patent is obvious.

(e) Copying

"Copying is an indicium of nonobviousness, and is to be given proper weight." *Diversitech Corp. v. Century Steps, Inc.*, 850 F.2d 675, 679 (Fed. Cir. 1988) (citing *Windsurfing International, Inc. v. AMF, Inc.*, 782 F.2d 995, 1000 (Fed. Cir.) ("the district court correctly noted that copying the claimed invention, rather than one within the public domain, is indicative of non-obviousness."); *see also Vandenberg v. Dairy Equip. Co.*, 740 F.2d 1560, 1567 (Fed. Cir. 1984) ("The copying of an invention may constitute evidence that the invention is not an obvious one.) (citation omitted); *Ortho-McNeil*, 348 F. Supp. 2d at 759 ("The copying of an invention may constitute evidence that the invention is not an obvious one.")

The Court concludes that there is also sufficient evidence that Teva has sought to copy Singulair®. The record shows that in connection with its ANDA Nos. 78-605 and 78-723, Teva submitted almost the identical labeling and package inserts as those contained in corresponding Singulair® products proposed montelukast sodium and chewable tablets. (Revised Final Pretrial Order, Stipulated Facts 6, 14; TEX 3003.0080; TEX 3009; TEX 3004.0001, 0009). This is sufficient evidence to demonstrate that Teva is attempting to copy Singulair®'s products and capitalize on these products success. As such, this factor also weighs against a conclusion that the '473 patent is obvious.

IV. CONCLUSION

For the foregoing reasons, the Court will deny MSD's Motion in Limine Regarding Deceptive Intent [Docket No. 64] and dismiss as moot MSD's Motion in Limine Regarding Dr. Jaffe's Expert Testimony Regarding : (1) the Ghostwriting of Scientific Articles Explaining the Safety and Efficacy of Singulair®; (2) and Evidence Pertaining to Neurotonin® and Nesiritide products. [Docket No. 70-2].

On the basis of the evidence introduced at trial, the Court also concludes that Teva has failed to prove either that: (1) MSD acquired the '473 patent through inequitable conduct or (2) the '473 patent was obvious under 35 U.S.C. § 103 in light of these additional prior arts. As such, the Court concludes that the '473 patent is valid and enforceable and that Teva's ANDA Nos. 78-605 and 78-723 infringe claims 18-22 of the '473 patent.

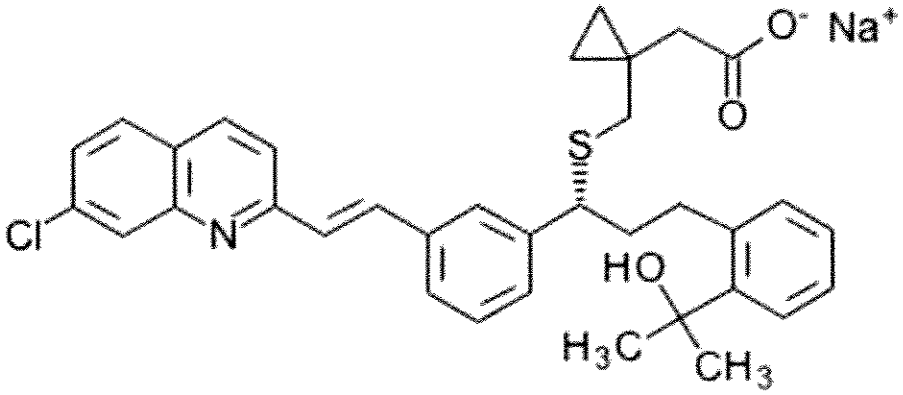
An appropriate form of order accompanies this opinion.

Dated: August 19 , 2009

/s/ Garrett E. Brown, Jr.
GARRETT E. BROWN, JR., U.S.D.J.

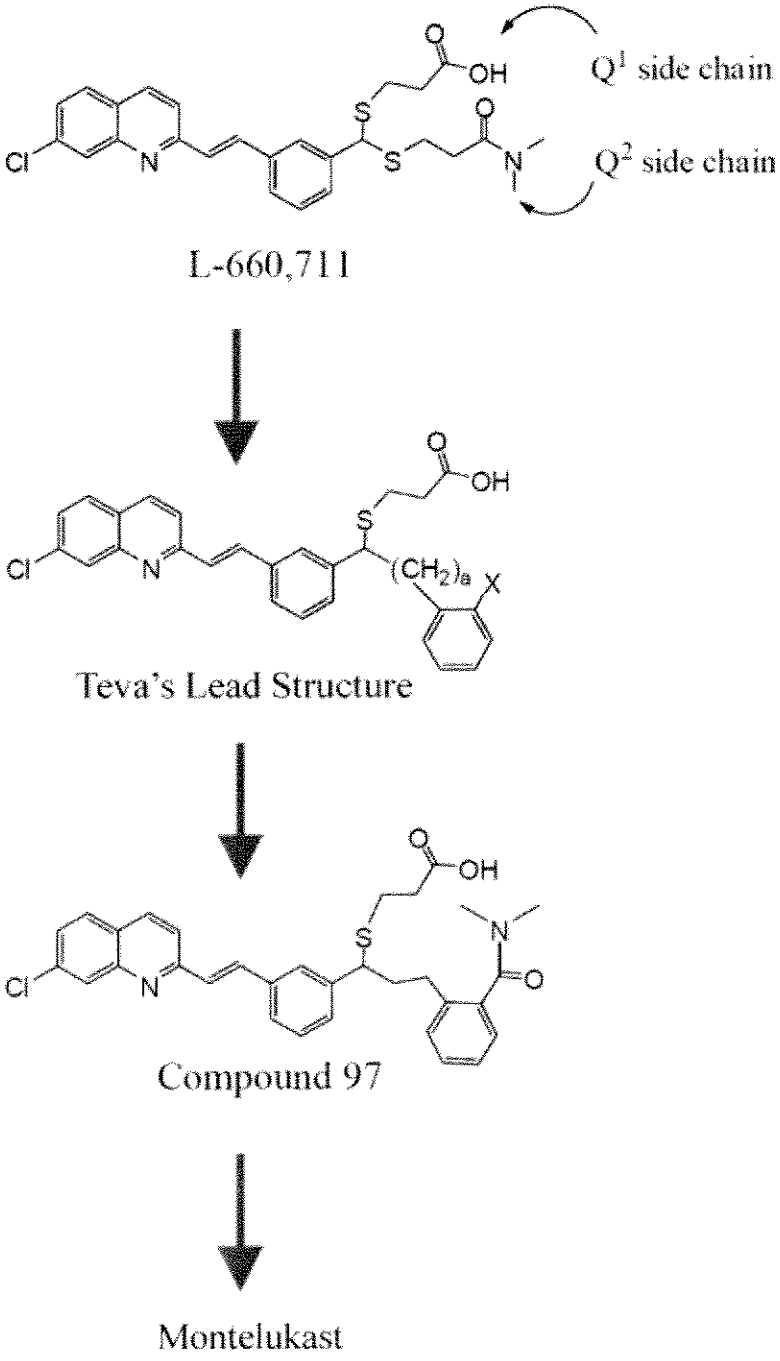
Appendix A

Figure 1



Montelukast

Figure 2


Q1 side chain
Q2 side chain
L-660,711
Teva's Lead Structure
Compound 97
Montelukast